**Ministry of Health, Singapore**
College of Medicine Building
16 College Road
Singapore 169854

Tel (65) 6325 9220
Fax (65) 6244 1677

www.moh.gov.sg

ISBN 978-981-09-0767-9

Academy of Medicine,
Singapore

# Attention Deficit Hyperactivity Disorder

## AMS-MOH Clinical Practice Guidelines 1/2014

Chapter of Psychiatrists
Academy of Medicine,
Singapore

College of Family
Physicians Singapore

College of Paediatrics and
Child Health, Singapore

MINISTRY OF HEALTH
SINGAPORE

**May 2014**

# Levels of evidence and grades of recommendation

**Levels of evidence**

| Level | Type of Evidence |
|---|---|
| **$1^{++}$** | High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias |
| **$1^{+}$** | Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias |
| **$1^{-}$** | Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias |
| **$2^{++}$** | High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal |
| **$2^{+}$** | Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal |
| **$2^{-}$** | Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal |
| **3** | Non-analytic studies, e.g. case reports, case series |
| **4** | Expert opinion |

**Grades of recommendation**

| Grade | Recommendation |
|---|---|
| **A** | At least one meta-analysis, systematic review of RCTs, or RCT rated as $1^{++}$ and directly applicable to the target population; or<br>A body of evidence consisting principally of studies rated as $1^{+}$, directly applicable to the target population, and demonstrating overall consistency of results |
| **B** | A body of evidence including studies rated as $2^{++}$, directly applicable to the target population, and demonstrating overall consistency of results; or<br>Extrapolated evidence from studies rated as $1^{++}$ or $1^{+}$ |
| **C** | A body of evidence including studies rated as $2^{+}$, directly applicable to the target population and demonstrating overall consistency of results; or<br>Extrapolated evidence from studies rated as $2^{++}$ |
| **D** | Evidence level 3 or 4; or Extrapolated evidence from studies rated as $2^{+}$ |
| **GPP** (good practice points) | Recommended best practice based on the clinical experience of the guideline development group. |

CLINICAL PRACTICE GUIDELINES

# Attention Deficit Hyperactivity Disorder

AMS-MOH Clinical Practice Guidelines 1/2014

Published by Ministry of Health, Singapore
16 College Road,
College of Medicine Building
Singapore 169854

Printed by Asiapak Pte Ltd



ISBN 978-981-09-0767-9

Available on the MOH website: http://www.moh.gov.sg/cpg

## Statement of Intent

These guidelines are not intended to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.

The contents of this publication are guidelines to clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not ensure a successful outcome in every case. These guidelines should neither be construed as including all proper methods of care, nor exclude other acceptable methods of care. Each physician is ultimately responsible for the management of his/her unique patient, in the light of the clinical data presented by the patient and the diagnostic and treatment options available.

# Contents

# Foreword

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder that is considered by the World Health Organisation (WHO) as a public health issue because of its prevalence and high disease burden. It is a condition which is seen by different professionals ranging from teachers to paediatricians, psychiatrists and family physicians. The management of ADHD has also received much media attention in the West for the overuse of stimulant medications.

Although the prevalence of ADHD in Singapore has been estimated to be less than 5%,[*] ADHD is the fourth-highest contributor to disease burden (as measured in disability-adjusted life years) in children aged 14 and below.[†] ADHD is increasingly being recognised for its impact on academic performance and social functioning. With the development of a comprehensive community mental health programme in schools called REACH (Response, Early Intervention and Assessment in Community Mental Health) by the Ministry of Health, Ministry of Education, Ministry of Social and Family Development and the National Council of Social Services working collaboratively, the pick-up rate for ADHD has doubled.

Clinical practice guidelines help professionals understand the evidence-based treatments that are available. These guidelines are designed with the medical and allied health professionals in mind but can also serve to inform educationists and parents on evidence-based treatments.

ASSOCIATE PROFESSOR BENJAMIN ONG
DIRECTOR OF MEDICAL SERVICES

---

[*] Woo, B.S.C., Ng, T.P., Fung, D.S.S., Chan, Y.H., Lee, Y., Koh, J.B.K., & Cai, Y., 2007. Emotional and behavioural problems in Singaporean children based on parent, teacher and child reports. [*]*Singapore Medical Journal*, 48 (12): 1100-106.

[†] Ministry of Health, Singapore. Singapore's burden of disease and injury 2010. Singapore: Ministry of Health; (pending publication).

# Executive summary of recommendations

Details of recommendations can be found in the main text at the pages indicated.

## Definition and diagnostic classification

**B** A diagnosis of attention deficit hyperactivity disorder should be made through a thorough clinical assessment, which should include an interview with the parent or significant caregiver of the child (pg 12).

**Grade B, Level 2++**

**B** When diagnosing attention deficit hyperactivity disorder, in addition to information from interviews with parents or caregivers, information from another adult who has interacted with the child in another setting (e.g. school teachers) should also be obtained (pg 12).

**Grade B, Level 2++**

**B** Before diagnosing attention deficit hyperactivity disorder (ADHD), a careful evaluation to exclude psychiatric or medical conditions which can account for ADHD-like symptoms should be performed (pg 12).

**Grade B, Level 2++**

**B** Attention deficit hyperactivity disorder is a diagnosis that should be considered when a pre-schooler presents with disruptive behaviour (pg 13).

**Grade B, Level 2++**

**C** The clinician should assess a child diagnosed with attention deficit hyperactivity disorder for co-morbid conditions (pg 13).

**Grade C, Level 2+**

**C** If there is a suspected learning disorder, appropriate psycho-educational or speech and language assessments should be sought from the appropriate specialists (pg 13).

**Grade C, Level 2+**

**A** There is no need for investigations such as thyroid function test, lead level or brain imaging to be done when assessing a child for attention deficit hyperactivity disorder, unless there is another medical indication (pg 14).

**Grade A, Level 1+**

**A** Electroencephalogram is not recommended as a diagnostic tool for attention deficit hyperactivity disorder in clinical practice (pg 15).

**Grade A, Level 1+**

## Overview of treatment for ADHD

**D** Clinicians who treat adolescents with attention deficit hyperactivity disorder should plan for the transition to adult health services in advance, discuss this with the patients and their families, and ensure that they can continue to receive care (pg 17).

**Grade D, Level 4**

## Psychosocial/alternative/complementary interventions

**B** After diagnosis, doctors should provide appropriate education about attention deficit hyperactivity disorder to children, families and teachers (pg 18).

**Grade B, Level 1+**

**A** Doctors should consider educating parents of children with attention deficit hyperactivity disorder about behaviour management strategies, or refer them to professionals who can do so [e.g. psychologists] (pg 19).

**Grade A, Level 1++**

**B** Parent training should be offered for parents of pre-school children with attention deficit hyperactivity disorder (pg 20).

**Grade B, Level 1+**

**B** Doctors should consider referring parents of children and adolescents with attention deficit hyperactivity disorder for parent training programmes offered within the community, particularly when negative parenting practices are identified (pg 20).

**Grade B, Level 1+**

**D** During the delivery of parent training, the professional should consider the use of behaviour management strategies which are more likely to be acceptable to the parents, based on an understanding of their cultural background (pg 21).

**Grade D, Level 3**

**GPP** Family therapy may be considered for the family of a child or adolescent with attention deficit hyperactivity disorder if severe disruption in relationships within the family is evident (pg 21).

**GPP**

**C** Academic interventions should be considered for the child with attention deficit hyperactivity disorder and should be made in consultation with educational professionals who work closely with the child in the learning or school context. [Guidelines for communications between the physician and the child's school are provided in Annex 5.] (pg 22).

**Grade C, Level 2+**

**GPP** Parents and caregivers should be encouraged to actively share information about the child's attention deficit hyperactivity disorder condition with his school, and collaborate with professionals and teachers in preparing the child for the educational setting (pg 24).

**GPP**

**B** Social skills training alone is not recommended for the management of attention deficit hyperactivity disorder (pg 25).

**Grade B, Level 1+**

**B** Cognitive-behavioural therapy alone is not recommended for the management of attention deficit hyperactivity disorder (pg 25).

**Grade B, Level 1+**

**B** There is no clear evidence for food additives and sugars to be related to attention deficit hyperactivity disorder. Parents and children should be advised to control food items containing additives or high sugar content that have been observed to consistently provoke physical or behavioural reactions (pg 26).

**Grade B, Level 1+**

**C** A restrictive elimination diet is not recommended for the management of attention deficit hyperactivity disorder (pg 27).

**Grade C, Level 2++**

**B** Omega-3 supplementation may be used as an adjunctive treatment for attention deficit hyperactivity disorder (pg 27).

**Grade B, Level 1+**

**B** Neurofeedback should not be used alone for the treatment of attention deficit hyperactivity disorder (pg 29).

**Grade B, Level 1+**

**A** Cognitive remediation alone is not recommended for the treatment of attention deficit hyperactivity disorder with significant impairment (pg 29).

**Grade A, Level 1+**

**D** A referral to an Occupational Therapist may be considered for children with sensory processing or motor skill deficits in addition to attention deficit hyperactivity disorder (pg 30).

**Grade D, Level 3**

## Pharmacological treatment

**A** When medication is considered for the treatment of attention deficit hyperactivity disorder, methylphenidate should be considered first (pg 32).

**Grade A, Level 1+**

**B** Methylphenidate may be used for long term treatment of attention deficit hyperactivity disorder symptoms, although the benefits of treatment should be reviewed regularly (pg 32).

**Grade B, Level 1+**

**B** Drug holidays during treatment with methylphenidate may be considered in order to limit adverse effects. Attention deficit hyperactivity disorder symptoms and impairment during the non-medication days should be monitored (pg 33).

**Grade B, Level 1+**

**A** The height, weight and body-mass-index (BMI) of children receiving treatment with methylphenidate should be regularly monitored (pg 33).

**Grade A, Level 1++**

**D** The height, weight and body-mass-index (BMI) of children receiving treatment with methylphenidate should be monitored every 6 months. If there is concern about slowing of growth rate, the need for continued medication use should be reviewed and jointly decided with parents, and there may be a need to evaluate for other medical reasons explaining this (pg 33).

**Grade D, Level 4**

**B** During treatment with methylphenidate, start at a low dose and slowly titrate upwards according to the child's response, or adjust the timing of medication, to minimise short-term adverse effects (pg 34).

**Grade B, Level 1+**

**C** A careful personal and family history of cardiovascular disease should be taken before starting medication treatment for attention deficit hyperactivity disorder. Children with pre-existing cardiac problems should be referred to a cardiologist for evaluation before treatment with methylphenidate or atomoxetine is initiated (pg 34).

**Grade C, Level 2+**

**A** Methylphenidate may be used to treat attention deficit hyperactivity disorder in children with comorbid tic disorder but treatment should be stopped if the tics worsen following treatment (pg 35).

**Grade A, Level 1+**

**B** The use of methylphenidate should be considered when treating attention deficit hyperactivity disorder in the presence of co-morbid disruptive behavioural disorder (pg 35).

**Grade B, Level 1+**

**B** The use of an extended-release methylphenidate instead of immediate-release methylphenidate should be considered if there is concern about medication abuse. Medication use by these patients should be carefully monitored (pg 35).

**Grade B, Level 1+**

**A** Methylphenidate may be considered for the treatment of attention deficit hyperactivity disorder in individuals who have also been diagnosed with autistic spectrum disorder. Care should be taken to watch for side effects (pg 36).

**Grade A, Level 1+**

**A** Atomoxetine may be used for the treatment of attention deficit hyperactivity disorder symptoms when there is increased risk with methylphenidate use [e.g. high risk of abuse or diversion] (pg 37).

**Grade A, Level 1+**

**A** During treatment with atomoxetine, there should be periodic monitoring of growth (height and weight) and mental state (suicidal thinking). If there is concern about slowing of growth rate, the need for continued medication use should be reviewed and jointly decided with parents, and there may be a need to evaluate for other medical reasons explaining this (pg 37).

**Grade A, Level 1++**

**D** The height, weight and body-mass-index (BMI) of children receiving treatment with atomoxetine should be monitored every 6 months (pg 38).

**Grade D, Level 4**

**B** Atomoxetine may be used as first line treatment when there is comorbid attention deficit hyperactivity disorder and tic disorder (pg 38).

**Grade B, Level 1+**

**C** The combination of methylphenidate and atomoxetine should not be used for the treatment of attention deficit hyperactivity disorder symptoms (pg 40).

**Grade C, Level 2+**

**A** To improve treatment adherence, treatment should be individualised for each patient with attention deficit hyperactivity disorder, and the parents' and their child's preferences should be considered (pg 41).

**Grade A, Level 1+**

**A** The use of methylphenidate or atomoxetine in pre-schoolers should be considered only if psychosocial interventions have failed. Care should be taken to regularly assess response and monitor for side effects, so as to decide if medication should continue to be administered (pg 41).

**Grade A, Level 1++**

## Cost-effectiveness issues

**A** Although medication is a cost-effective treatment for attention deficit hyperactivity disorder (ADHD), treatment for ADHD should be individualised and other factors (e.g. presence of co-morbidity) should be considered before initiating medications (pg 42).

**Grade A, Level 1++**

# 1 Introduction

## 1.1 Background information

Attention deficit hyperactivity disorder (ADHD) is a neuro-developmental disorder, characterised by the presence of early-onset persistent, pervasive and impairing hyperactive-impulsive and/or inattentive symptoms. The worldwide pooled prevalence was about 5.29%.[1] While there has been no epidemiological study on the prevalence of this condition among children in Singapore, a local study reported the prevalence of externalising problems to be 4.9% among Singaporean primary school children.[2] While ADHD symptoms decline with age, a meta-analysis reported that a significant proportion might have residual symptoms in adulthood.[3] ADHD has been reported to be associated with negative outcomes including poor academic achievement, reduced self-esteem and higher smoking rate. This condition is often picked up when the child is young, and children with ADHD are often treated by child psychiatrists and paediatricians.

## 1.2 Objectives and scope of guideline

These guidelines are not meant to be viewed as a protocol, but rather, to provide a framework to:

- Approach the assessment process, with the goals of arriving at a diagnosis and planning treatment
- Inform the practitioner about the level of evidence for medication available in Singapore, to aid the decision about medication use
- Inform about the evidence for non-pharmacological treatment approaches to help professionals plan treatment and discuss these with parents

## 1.3 Target group

The target group of these guidelines are professionals who come into contact with children and adolescents below the age of 18 who have attention deficit hyperactivity disorder (ADHD). The information is intended to help professionals plan the treatment for such children and adolescents. Professionals should exercise caution when extrapolating the evidence beyond this stated age group.

## 1.4 Guideline development

These guidelines were produced by a multi-disciplinary workgroup appointed by the Academy of Medicine, Singapore. The workgroup comprised psychiatrists, paediatricians, educational psychologists, a medical social worker, a pharmacist, an advanced practice nurse and a parent representative.

## 1.5 Review of guidelines

Evidence-based clinical practice guidelines are only as current as the evidence that supports them. Users must keep in mind that new evidence could supersede recommendations in these guidelines. The workgroup advises that these guidelines be scheduled for review five years after publication, or earlier if new evidence appears that requires substantive changes to the recommendations.

# 2 Definition and diagnostic classification

## 2.1 Assessment

The Diagnostic and Statistical Manual of Diseases, 4th edition, text revised (DSM-IV TR) and International Classification of Diseases, 10th edition (or ICD-10) are used to guide the diagnosis of attention deficit hyperactivity disorder (ADHD). DSM-IV TR uses the term ADHD and further classifies into inattentive, hyperactive-impulsive and combined subtypes. More recently, an updated 5th edition of the DSM was published. ICD-10 uses the term 'hyperkinetic disorder' instead of ADHD.

Most clinical studies of ADHD use the DSM classification system. The DSM-IV TR criteria for the diagnosis of ADHD have been shown to be valid in a comprehensive review and meta-analysis, but validity for the subtypes is weaker.[4] DSM-IV TR requires an adequate number of criteria to be met, and for the symptoms to be pervasive (onset before age 7, in more than one setting), persistent (duration longer than 6 months) and to have caused significant impairment. ADHD is therefore a clinical diagnosis.

Around the time of preparation of these guidelines, the fifth edition of the DSM (DSM-V) has just been published. The main changes to the diagnostic criteria in DSM-V, compared to DSM-TV TR, are described below, with some discussion about their implications:

1. ADHD is now classified as a 'Neurodevelopmental Disorder', rather than being grouped together with externalising disorders such as Oppositional Defiant Disorder and Conduct Disorder (all 3 conditions are grouped together as 'disruptive behaviour disorders' in DSM-IV TR). This emphasises the need to focus on the detection of symptoms early in childhood and provide appropriate intervention.

2. The DSM-IV subtypes of ADHD are no longer differentiated. Instead, DSM-V emphasises the current clinical presentation of ADHD, which may be hyperactive-impulsive, inattentive or combined. This has arisen from research showing that ADHD symptoms may change over time (e.g. from predominantly combined symptoms to predominantly inattentive symptoms).

3. The age at symptom onset has been changed from before age 7 to before age 12. DSM-IV TR specified that some of the symptoms causing impairment must be present before age 7 but DSM-V requires some of the symptoms to be present before the age of 12 without emphasising on the impairment. Impairment from ADHD symptoms may sometimes not be evident in early childhood (e.g. impairment in academic achievement may only be evident later when academic demands are higher).

4. Autism Spectrum Disorder is no longer considered an exclusionary condition; thus, an individual may receive the dual diagnosis of ADHD and Autism. This emphasises the need for careful clinical evaluation for ADHD symptoms in this special needs group so that appropriate intervention can be provided to optimize their learning and functioning.

5. The clinical symptom threshold for ADHD in individuals aged 17 and older has been reduced from 6 symptoms of inattention or 6 of hyperactivity/impulsivity to 5 symptoms of either. Whereas DSM-IV TR provided only the criteria threshold for ADHD diagnosis in childhood, this change in symptom criteria reflects the different clinical presentation of ADHD in late adolescence and adulthood.

6. DSM-V retains the 18 symptom criteria but has provided additional examples for each symptom that are more relevant for older adolescents and adults than were the examples provided in DSM-IV. When assessing for ADHD symptoms in an older individual, the clinician should be aware of the differences in clinical presentation at an older age.

It cannot be further emphasised that ADHD should be recognised and treated early. As such, this set of guidelines will focus on the assessment and treatment of ADHD in children and adolescents In DSM-V, the age of onset for the diagnosis of ADHD was increased from the age of 7 to 12 years. This amendment largely arose from studies involving the diagnosis of ADHD in adult patients when there was difficulty obtaining retrospective information about the presence of ADHD symptoms prior to age seven. There were studies reporting that adults who were able to report symptom onset by age 12 also had symptoms by age 7, even if they could not report them, and that prevalence estimates, course of illness and medication response were not affected.[5-8]

When assessing children and adolescents in the local setting, it is often possible for parents to provide relevant history and to obtain previous school records, and effort should be spent to obtain evidence of the presence of symptoms early in childhood.

To obtain information about the child, it will be necessary to interview the parent or main caregiver. Studies have shown that children with ADHD may not accurately report their behavioural conduct and competence.[9] There is also evidence that using information from a single informant, such as parents, to diagnose ADHD may not be accurate.[10-13]

As the DSM-IV TR requires the presence of symptoms in more than one setting and resultant impairment, information should also be obtained from another adult, usually the child's school teacher.

The DSM-IV TR requires that the symptoms are not better accounted for by another psychiatric or medical condition. Some disorders which can present with ADHD-like symptoms are listed in Annex 1. As discussed, DSM-V allows the co-diagnosis of ADHD and autistic spectrum disorder.

There is increasing evidence that ADHD is a heritable condition with underlying genetic cause. There is insufficient evidence to implicate an environmental cause for most cases of ADHD.[14]

**B** A diagnosis of attention deficit hyperactivity disorder should be made through a thorough clinical assessment, which should include an interview with the parent or significant caregiver of the child.

**Grade B, Level 2++**

**B** When diagnosing attention deficit hyperactivity disorder, in addition to information from interviews with parents or caregivers, information from another adult who has interacted with the child in another setting (e.g. school teachers) should also be obtained.

**Grade B, Level 2++**

**B** Before diagnosing attention deficit hyperactivity disorder (ADHD), a careful evaluation to exclude psychiatric or medical conditions which can account for ADHD-like symptoms should be performed.

**Grade B, Level 2++**

## 2.2 Diagnosis of ADHD in pre-schoolers

There has been earlier concern whether ADHD should be diagnosed in pre-school children as many pre-schoolers may have some symptoms of ADHD but may not meet full diagnostic criteria for the disorder.[15] More recent studies have shown that the diagnosis of ADHD can be reliably made among children in this age group.[16] The DSM-IV criteria for ADHD were reported to have good concurrent and predictive validity: pre-school children diagnosed with DSM-IV ADHD experienced more academic and peer relationship difficulties[17] and the diagnosis was stable across time.[18,19] As with most neurodevelopmental disorders, an early diagnosis provides an opportunity for earlier intervention before the build-up of more severe negative consequences of untreated ADHD.

**B** Attention deficit hyperactivity disorder is a diagnosis that should be considered when a pre-schooler presents with disruptive behaviour.

**Grade B, Level 2++**

## 2.3 Co-morbidities of ADHD

ADHD often co-exists with another psychiatric disorder, with epidemiological studies reporting comorbidity rates as high as 50-90%.[4,9] Some of the more common comorbid disorders include oppositional defiant disorder, conduct disorder, learning disorder, anxiety disorder, mood disorder and smoking and substance use.[20-27] While ADHD can interfere with the child's availability for learning, it does not reduce the brain's ability to learn and therefore should not be considered as a learning disability per se.[28]

**C** The clinician should assess a child diagnosed with attention deficit hyperactivity disorder for co-morbid conditions.

**Grade C, Level 2+**

**C** If there is a suspected learning disorder, appropriate psycho-educational or speech and language assessments should be sought from the appropriate specialists.

**Grade C, Level 2+**

## 2.4 Use of questionnaires

Questionnaires are a useful way to obtain information from school teachers or other adults who know the child well, especially if a face to face interview is not possible. Such questionnaires usually have a parents' and a teachers' version and can be useful to obtain information about the presence of ADHD symptoms in various settings. As symptoms alone are inadequate for the diagnosis of ADHD as discussed earlier, the diagnosis of ADHD cannot be established solely based on information obtained from such questionnaires.

Subsequent repeated application of questionnaires can be useful to monitor the improvement of ADHD symptoms (e.g. to evaluate the child's response to treatment). Some of the commonly used rating scales which have been validated overseas and are widely used are listed in Annex 2.

ADHD questionnaires such as the Vanderbilt ADHD Diagnostic Parent Rating Scale may be helpful in screening for co-existing ODD, CD, anxiety, or depression.[29]

However, questionnaire results should be interpreted with caution as there is no ADHD-specific questionnaire which has established cut-off scores for our local population.

## 2.5 Other investigations

Studies which had investigated various laboratory investigations such as lead level and thyroid functions did not provide convincing evidence of their usefulness.[30, 31]

A review concluded that there was insufficient evidence to support the use of tests of such as lead levels, thyroid function and brain imaging to screen children suspected of having ADHD.[32]

**A** There is no need for investigations such as thyroid function test, lead level or brain imaging to be done when assessing a child for attention deficit hyperactivity disorder, unless there is another medical indication.

**Grade A, Level 1+**

Neurophysiological studies have suggested that children with ADHD exhibit specific brain wave patterns on the electroencephalogram (EEG), which distinguish them from normal children. Approximately 85–90% of patients with ADHD exhibit under activity over frontal and central, midline cortical regions.[33]

The primary electrophysiological indicators of under activity identified via quantitative electroencephalographic (QEEG) analysis of patients with ADHD include: elevated relative theta power, reduced relative alpha and beta power, and elevated theta/alpha and theta/beta power ratios.[34]

Two reviews had found increased frontocentral theta band activity and increased theta to beta ($\theta/\beta$) power ratio during rest, as the most common finding in ADHD, compared to non-ADHD controls.[35,36] However, a recent meta-analysis of nine studies concluded that elevated theta-beta ratios cannot be considered a reliable diagnostic measure of ADHD.[37]

Two studies had also highlighted some of the problems in using EEG as a diagnostic test for ADHD.[38, 39]

**A** Electroencephalogram is not recommended as a diagnostic tool for attention deficit hyperactivity disorder in clinical practice.

**Grade A, Level 1+**

Infra-red technology has also been applied to assess head movement in two small case-control studies, and more studies are necessary before their value as a diagnostic tool can be determined.[40, 41]

Actigraphy has also been used to assess activity level during the daytime, sleep and over 24 hours. There were both positive and negative studies, and more research is needed to determine their utility in clinical practice.[42-45]

There is insufficient evidence to recommend the use of actigraphy or infra-red motion analysis during assessment for ADHD.

## 3 Overview of treatment for ADHD

In the late 1990s, the multimodal treatment for ADHD, or MTA trial, a multi-site randomised controlled trial, was planned to provide answers regarding the efficacy of the most evidenced-based treatment for ADHD.[46]

The main treatment arms included medication, intensive behaviour treatment and a combination of both medication and intensive behaviour treatment. The last arm was 'community treatment' which represented 'treatment as usual'.

The following sections will discuss the evidence for the various treatment options for ADHD will therefore be divided into pharmacological and non-pharmacological treatment. Non-pharmacological treatment can be grouped into psychosocial or behavioural treatment, and complementary or alternative treatment. There is evidence that many parents prefer to avoid the use of medication.[47]

When deciding on the choice of treatment, several factors need to be considered. The age of the child is important, as younger children particularly pre-schoolers, tend to experience more side effects with medication and non-pharmacological treatment may be considered first. The preferences of the parents and the children themselves will also need to be considered, particularly if the children are older and their co-operation will be required for treatment to be carried out.

Some of the treatment options may be available within the community (e.g. parenting programme) but may not be available at regular fixed schedules so networking among the professionals is important to keep one another updated about the availability of resources. For example, parents may be informed about the local parent support group SPARK (Society for the Promotion of ADHD Research and Knowledge) which is also active in providing caregiver education and support.

## 3.1 Care transition

The importance of transition from child to adult health services, in the treatment of ADHD, has been highlighted by the NICE guidelines.[48]

However surveys have suggested that there is a lack of structured guidelines on the transition process and often little communication between child and adult services.[49, 50]

This process also needs to take into account the healthcare system and available professional mental health services. In particular, clinicians need to consider Singaporean adolescent males who need to perform National Service.[51]

**D** Clinicians who treat adolescents with attention deficit hyperactivity disorder should plan for the transition to adult health services in advance, discuss this with the patients and their families, and ensure that they can continue to receive care.

**Grade D, Level 4**

# 4 Psychosocial / alternative / complementary interventions

## 4.1 Psychosocial interventions

Overall, there is relatively limited research on psychosocial interventions for adolescents with ADHD, and the strategies discussed below are largely tailored for children.

### 4.1.1 Education about ADHD

Education about ADHD involves the provision of information on ADHD diagnosis, assessment, treatment options and general advice on improving behavioural outcomes. This has also been referred to as 'psychoeducation' by mental health professionals.

The aim of the education is to encourage symptom recognition, allow active participation in treatment, enhance adherence to treatment and to provide patients and families with coping skills.[52] Such education has been shown to improve a child's behaviour, parent and child satisfaction, child's knowledge of ADHD, child's opinion of medications, adherence to medical recommendations and teacher knowledge.[53-57]

A systematic review concluded that the available evidence for the approach to provide education about ADHD was considered limited due to the methodological limitations of available studies.[58] In a small controlled trial involving school-aged children aged 7-12 at a primary care facility, those who received group education about ADHD had improved behavioural ratings from parents, but not from teachers.[59]

**B** After diagnosis, doctors should provide appropriate education about attention deficit hyperactivity disorder to children, families and teachers.

**Grade B, Level 1+**

### 4.1.2 Behavioural intervention

Behavioural interventions are aimed at modifying antecedents and/or consequences, in order to change behaviour. Antecedents describe events or factors that precede behaviour (e.g. presence of clear rules, communication

style). Consequences describe events that follow a behaviour which can have the effect of either increasing or decreasing the likelihood that the behaviour will happen again in the future. Positive consequences (e.g. reward) increase the likelihood that behaviour will happen again, whereas negative consequences (e.g. withdrawing a privilege) and punishment decreases the likelihood that behaviour will happen again.

Behavioural interventions are usually taught to caregiving adults (parents as part of parent training, school teachers as part of classroom management) and are recommended by most guidelines. This involves working with parents and teachers to program behavioural contingencies into the child's home, school, and recreational environments.[60] Many parents also prefer behavioural interventions over medication.[61]

#### 4.1.2.1 Intensive training programme

The Summer Treatment Programme is an intensive, 8-week outpatient programme that includes weekly group-based parent training, a token or point system, positive reinforcement, effective commands, time out, social skills training, sports skills training, and problem solving skills training. It is also one component of the intensive behaviour treatment used in the MTA study. These treatment components are implemented across recreational and academic settings.[62] Uncontrolled and controlled studies have reported significant improvement in ratings of ADHD symptoms, peer relationships and overall functioning by parents and programme teachers and counsellors.[63, 64]

A recent controlled open-label trial using a 2-week programme consisting of a social skills training programme and parent education and training programme reported improvement in ADHD symptoms, peer relationships, and overall functioning of children.[65] However, the actual effectiveness of the individual component of the programme is not clear. The amount of resources required can make the full programme challenging to implement.

**A** Doctors should consider educating parents of children with attention deficit hyperactivity disorder about behaviour management strategies, or refer them to professionals who can do so (e.g. psychologists).

**Grade A, Level 1++**

### 4.1.3 Parent training

Within families with children diagnosed with ADHD, parent-child relationships are often disrupted.[66] The child's behaviour can influence parents to adopt more controlling/negative parenting practices.[67] These parents also experience significant parenting stress and psychopathology.[66] Changing parental practice and improving parent-child interactions can lead to better outcomes for both parents and child.[68] Several well-studied parenting programmes for ADHD include the Triple P Positive Parenting Programme and the Incredible Years Programme.

Parent training has consistently been evaluated as an evidence-based intervention, and has been recommended as first-line treatment for a young child.[63, 69, 70] One meta-analysis found parent training to be more effective than methylphenidate for treatment of pre-schoolers at risk for ADHD.[71] One review noted that a small number of studies involving adolescents showed equivocal results.[63] Parent training programmes have also been shown to be cost-effective, and the positive effects can persist even after 2-5 years.[72, 73]

However, a recent Cochrane review of randomised controlled trials of parent training for ADHD among those aged 5 to 18 concluded that most trials were of poor methodological quality and hence, there was insufficient evidence to recommend parent training to improve ADHD-specific behaviour and academic outcomes.[74]

One local study did not find an association between children's behaviour problems and negative parenting. The case-control study cautioned about the need to consider cultural factors, especially when most parenting studies and programmes are conducted in the Western population.[75]

**B** Parent training should be offered for parents of pre-school children with attention deficit hyperactivity disorder.

**Grade B, Level 1+**

**B** Doctors should consider referring parents of children and adolescents with attention deficit hyperactivity disorder for parent training programmes offered within the community, particularly when negative parenting practices are identified.

**Grade B, Level 1+**

**D** During the delivery of parent training, the professional should consider the use of behaviour management strategies which are more likely to be acceptable to the parents, based on an understanding of their cultural background.

**Grade D, Level 3**

**GPP** Family therapy may be considered for the family of a child or adolescent with attention deficit hyperactivity disorder if severe disruption in relationships within the family is evident.

**GPP**

### 4.1.4 Classroom behaviour management

Behaviourally based classroom interventions involve regular consultation with the child's teacher regarding the use of behaviour modification strategies. Therapists may provide recommendations to teachers regarding the use of specific behavioural techniques, including praise, planned ignoring, effective commands, and time out, as well as the daily report card[60] and individualised or classroom-wide contingency management strategies.

Several reviews concluded that while many studies show positive results, methodological limitations exist. Many studies utilised single-subject designs or group designs that included either a wait-list or a no-treatment control group, did not use blinded raters, had co-interventions and there were few studies involving pre-school children.[63, 76, 77]

Practical challenges exist during implementation and as such close and regular communication between the school, parents and clinicians will be necessary. Also some of the strategies were implemented in classroom contexts with small student-to-teacher ratio, and these may be difficult to implement in larger group settings.

### 4.1.5 Academic interventions

A diagnosis of ADHD on its own does not imply that a child has co-morbid learning difficulties or learning disorders. However, children with ADHD are at-risk of academic underachievement and are more likely to have academic problems than their peers without ADHD.[78, 79]

A meta-analysis of seven studies concluded that pharmacological treatment alone does not significantly improve academic achievement among children with ADHD.[80] There is thus the need for academic interventions to be in place to address learning issues.[21, 81]

School-based interventions, including behaviour management techniques, made in consultation with professionals who can observe the child frequently in his or her daily teaching and learning environment e.g. school teachers, psychologists, counsellors have been shown to improve academic functioning.[55, 82-84]

**C** Academic interventions should be considered for the child with attention deficit hyperactivity disorder and should be made in consultation with educational professionals who work closely with the child in the learning or school context. (Guidelines for communications between the physician and the child's school are provided in Annex 5)

**Grade C, Level 2+**

### 4.1.5.1 Classroom and curricular accommodations

The use of functional behaviour assessment can identify the triggers or antecedents of the children's negative behaviours in the classroom and be used as a basis to make recommendations on classroom and curricular accommodations to reduce the negative behaviour and improve learning.[85]

The child's functional deficits and the appropriate accommodations would need to be determined in consultation with professionals, who work closely with the child in his daily learning environment.

There is concern that long-term use of these accommodations may unnecessarily lower the academic expectations on the affected children and reduce their opportunities for skill development and remediation of deficits.[89, 90] As such, even with the use of curricular accommodations, interventions to remediate the academic skill deficits should continue. For example, while it may be appropriate for a class teacher to provide notes to a student with ADHD for a limited period of time, it would be important for this student to practise note-taking skills, and that the teacher eventually tapers this accommodation, and increases student participation.

### 4.1.5.2 Peer-mediated interventions

Several models of peer tutoring have been investigated with the population of students with ADHD.

Most models were (a) working one-to-one with another individual; (b) the learner determining instructional pace; (c) continuous prompting of academic responses, and (d) providing frequent, immediate feedback about quality of performance. These showed positive effects for enhancing students' academic performance in mathematics, reading and spelling.[91-93]

### 4.1.5.3 Computer-assisted instruction (CAI)

Computerized training in working memory can bring about significant gains in academic performance in core academic skills.[94, 95]

Computer-assisted instruction (CAI) is a method that allows teachers to provide students with opportunities to review and practise lesson materials independently.

CAI can enhance presentation of instructional material and improve students' motivation and academic achievement. Small studies involving children with ADHD have shown it improves oral reading fluency[96] and basic mathematics computation skills.[97]

### 4.1.5.4 Access arrangements

Access arrangements are pre-agreed reasonable adjustments that are made to examinations, tests and assessments in certain subjects for individual candidates. Some examples of these adjustments are extended time, modification of examination papers, and exemption from a component of a subject e.g. oral examination. These adjustments may be restricted in certain subjects.

Access arrangements are granted to ensure that candidates with special needs have access to national examinations, by giving them the opportunity to demonstrate their skills and abilities and receive recognition for their academic achievements.

The diagnosis of ADHD alone is insufficient for the approval of access arrangements during national examinations. Not every student with ADHD needs access arrangements, nor do all students with ADHD need the same type of access arrangement. Extended time for examinations does not necessarily benefit all children with ADHD.[87, 88]

Recommendations for access arrangements should be accompanied by clear and current evidence of needs and functional impairments to demonstrate that the access arrangements recommended would be effective and appropriate.

The evaluation of the student's current learning needs arising from the ADHD should be carried out by a qualified professional, such as a Psychiatrist, Educational Psychologist and Child/Clinical Psychologist.

**GPP** Parents and caregivers should be encouraged to actively share information about the child's attention deficit hyperactivity disorder condition with his school, and collaborate with professionals and teachers in preparing the child for the educational setting.

**GPP**

### 4.1.6 Social skills training

A recent Cochrane review examined 11 randomised trials involving children aged 5 to 12, with a wide range of intervention duration ranging from 8 to 10 weeks (8 trials) up to 2 years. The content of the social skills interventions was based on a cognitive-behavioural model. Most trials compared social skills training and parent training plus medication versus medication alone. Overall, the trials had high risk of bias. The meta-analysis found no statistically significant treatment effects on social skills competences, teacher-rated general behaviour or ADHD symptoms.[98]

In one large RCT examining young children with ADHD (ages 7–9) but free of conduct and learning disorders, those randomised to receive methylphenidate plus multimodal psychosocial treatment that included social skills training, did not do better in social functioning measures, compared to those who received methylphenidate alone, or methylphenidate plus attention control treatment.[99]

A locally developed 9-lesson, group-based social problem-solving skills training programme showed efficacy in reducing disruptive behaviour, but is currently being investigated in a randomised controlled trial.[100]

Overall, no adverse events were reported in studies. It is more acceptable to parents than medication as an early intervention. It is also low cost, and has been incorporated as part of some out-of-clinic peer-group interventions.

**B** Social skills training alone is not recommended for the management of attention deficit hyperactivity disorder.

**Grade B, Level 1+**

### 4.1.7 Psychological intervention

Randomised controlled trials of cognitive-behavioural treatment (CBT) for children with ADHD did not find it to be useful in reducing ADHD symptoms.[101, 102]

A recent uncontrolled trial of CBT among adolescents with ADHD, most of whom were treated concurrently with medication, found that those with co-morbid oppositional defiant disorder or conduct disorder did not benefit from treatment.[103]

A review of research into psychosocial treatment approaches for ADHD summarized that there is limited evidence that cognitive-behavioural therapy is efficacious in the treatment of ADHD in children.[104]

**B** Cognitive-behavioural therapy alone is not recommended for the management of attention deficit hyperactivity disorder.

**Grade B, Level 1+**

## 4.2 Diet and food substances

### 4.2.1 Food colouring and benzoate preservatives

One large controlled study of normal children aged 3 years examined the effect of a diet eliminating artificial colourings and benzoate preservatives. There was only improvement in parent-rated behaviour but not in the other more objective outcomes.[105]

In a randomised, double-blinded, placebo-controlled, crossover trial, artificial food colourings and benzoate additives worsened hyperactivity among normal children aged 3 years and 8/9 years, based on aggregated scores of observed behaviours and ratings by teachers and parents, plus, for 8/9-year-old children, a computerised test of attention.[106]

A meta-analysis of high-quality studies confined to colour additives showed a reliable overall positive effect in behaviour and psychometric tests of attention when these were removed from the child's diet, but commented that these studies were susceptible to publication bias and may involve non-generalizable samples. It estimated that 8% of children with ADHD may have symptoms related to synthetic food colours.[107]

### 4.2.2 Sugars

One meta-analysis concluded that sugar does not affect the behaviour or cognitive performance of children.[108] However, similar to the earlier view on dietary effects, it concluded that a small effect of sugar or effects on subsets of children cannot be ruled out.

**B** There is no clear evidence for food additives and sugars to be related to attention deficit hyperactivity disorder. Parents and children should be advised to control food items containing additives or high sugar content that have been observed to consistently provoke physical or behavioural reactions.

**Grade B, Level 1+**

### 4.2.3 Restricted elimination diet

A more extreme diet restriction to eliminate hyperallergenic food from a child's diet has been investigated. One recent open-label randomised controlled trial investigated a 5-week few-foods diet (rice, meat, vegetables, pear, water etc.) complemented with specific foods such as potatoes, fruit and wheat, among children aged 4 to 8. A subset of children who did not show response after 2 weeks were further restricted in their diet. There was significant improvement in ADHD symptoms compared to those who were not on any dietary control.

A restrictive diet is time consuming, disruptive to the household and becomes challenging to implement in older children. There is also concern over potential nutritional deficiency.[109, 110]

**C** A restrictive elimination diet is not recommended for the management of attention deficit hyperactivity disorder.

**Grade C, Level 2++**

## 4.2.4 Supplementation

### 4.2.4.1 Omega-3 supplementation

The main omega-3 fatty acids are eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and alpha-linolenic acid (ALA).

Studies involving omega-3 studies are heterogeneous in their choice of patient group, the type and dose of fatty acid employed, addition of anti-oxidant, choice of placebo (which may have small effects on behaviour), duration of treatment and outcome measurement. The heterogeneity is likely to have influenced the variable responses and results among these studies.

One meta-analysis of 10 trials involving 699 participants reported a small effect of omega-3 fatty acid supplementation on ADHD and that higher doses of EPA were more effective.[111]

One randomised controlled trial compared the effects of dietary supplementation with omega-3 and omega-6 (in a ratio of 80% to 20%) to placebo in 117 children with developmental coordination disorder. No child had a clinical diagnosis of ADHD but one-third was reported to have significant ADHD symptoms. In the intervention group, there was not only improvement in reported ADHD symptoms, but in reading and spelling skills as well.[112]

**B** Omega-3 supplementation may be used as an adjunctive treatment for attention deficit hyperactivity disorder.

**Grade B, Level 1+**

#### 4.2.4.2 Zinc and iron supplementation

Three double-blind, placebo controlled studies were available for zinc. The first Turkish study found small positive effects of zinc supplementation in reducing hyperactive, impulsive and impaired socialization symptoms, but not inattentive symptoms.[113] A small (n=44) 6-week study found greater improvement in reported ADHD symptoms among children taking methylphenidate with zinc supplementation (15 mg zinc supplementation/day), compared to those taking methylphenidate with a placebo.[114] The third study examining 2 doses of zinc supplementation (15 mg and 30 mg zinc/day) did not find any consistent improvement.[115] A review of these 3 studies concluded that the third study was the only trial that was well controlled and randomised according to the baseline zinc level; it showed that using zinc, either alone or in combination with stimulants, did not improve ADHD.[116] Another review questioned the generalisability of positive studies which were mostly done in areas with suspected endemic zinc deficiency.[117]

One small placebo-controlled study found that iron supplementation in deficient (serum ferritin levels <30 ng/mL) children with ADHD improved ADHD symptoms.[118]

There is insufficient evidence to recommend zinc and iron supplementation for the treatment of ADHD.

## 4.3 Alternative treatments

### 4.3.1 Neurofeedback

Neurophysiological studies have shown children with ADHD to have different EEG patterns compared with peer-aged subjects.[33,119,120] Neurofeedback therapy (or neurotherapy) trains the individual to alter their EEG rhythm.

Although some reviews supported the positive results reported in many controlled trials,[121-123] other reviews conducted of published studies have criticised the methodological quality of the studies investigating neurofeedback.[124-126]

**B** Neurofeedback should not be used alone for the treatment of attention deficit hyperactivity disorder.

**Grade B, Level 1+**

### 4.3.2 Cognitive remediation

There is evidence that working memory performance is impaired in children with ADHD.[127,128] It has therefore been hypothesised that computer-based training may improve working memory capacity in ADHD and become further generalised into other settings and everyday tasks.[94,129] One commonly studied cognitive remediation or training programme is the Cogmed Working Memory Training. Several reviews of studies, as well as recent randomised controlled trials examining cognitive remediation training for children with ADHD did not show consistent improvement in cognitive functions or ADHD symptoms.[130] Other reviews similarly concluded that the evidence for cogmed and cognitive training in ADHD is inconclusive.[131] Another recent review and several randomised controlled trials did not show cogmed working memory training to reduce ADHD symptoms or show generalised improvement in other functional domains.[132,133] Most studies also did not have a follow-up period of more than 6 to 8 months after completion of training, and there is a lack of longer term data to inform on the persistence of any improvement.[134, 135]

**A** Cognitive remediation alone is not recommended for the treatment of attention deficit hyperactivity disorder with significant impairment.

**Grade A, Level 1+**

## 4.4 Other therapies

### 4.4.1 Occupational therapy

Several case series have reported that some children with ADHD may have sensory processing or motor skill deficits.[136,137]

The American Academy of Pediatrics recommends that there should be regular monitoring of treatment effect for a child receiving sensory-based therapy, as there is limited data on the use of sensory-based therapies for childhood developmental and behavioural problems.[138]

**D** A referral to an Occupational Therapist may be considered for children with sensory processing or motor skill deficits in addition to attention deficit hyperactivity disorder.

**Grade D, Level 3**

### 4.4.2 Traditional Chinese Medicine (TCM)

A systematic review concluded that there was a lack of high quality clinical trial to support the recommendation of any particular kind of TCM preparation for treating ADHD in children.[139]

There is insufficient evidence to recommend any particular TCM preparation for the treatment of ADHD.

### 4.4.3 Acupuncture

A review identified 3 randomised controlled trials suitable to assess the effectiveness of acupuncture for treating ADHD.[140] One trial found that electro-acupuncture plus behavioural treatment was superior to sham electro-acupuncture plus behavioural treatment among pre-school children.[141] The review assessed the two other trials to have severe methodological flaws which limited their generalisability.

A Cochrane review also concluded that there is inadequate evidence to draw any conclusions about the efficacy or safety of acupuncture for ADHD in children and adolescents.[142]

There is insufficient evidence to recommend acupuncture for the treatment of ADHD.

### 4.4.4 Other interventions

Some other interventions which have been investigated in small studies include massage,[143,144] relaxation training[145] and hypnotherapy.[146] There is insufficient evidence to recommend these approaches for treatment at present.

One small study investigated music therapy in 18 aggressive youth aged 11-15 in a residential villa (12 had previously-diagnosed ADHD). While no significant treatment effects were found, increased disruptive behaviour in the classroom was found among those with ADHD.[147]

## 5 Pharmacological treatment

Most treatment studies involve school-aged children, rather than adolescents. This section will focus on pharmacological treatment for pre-schoolers, school-aged children and adolescents. Pharmacological agents used in children with ADHD include:

a) Stimulants (e.g. methylphenidate, amphetamine such as mixed amphetamine salts, dexamphetamine)

b) Non-stimulants
- Selective norepinephrine reuptake inhibitors (e.g. stomoxetine)
- α2-agonists [clonidine, guanfacine]
- bupropion
- Tricyclic antidepressants [imipramine, desipramine, nortriptyline]
- Others [modafinil, pemoline]

Stimulant medications, atomoxetine, guanfacine (Kapvay) and clonidine (Intuniv) are approved by the United States Food and Drug Administration (FDA) for the treatment of ADHD. For ease of reference by doctors, Annex 3 provides some information about these medications which are available in Singapore. This information is also available in the medications' package inserts.

The main groups of medication licenced by the Health Science Authority of Singapore and the United States Food and Drug Administration for the treatment of ADHD include stimulant medications such as methylphenidate and non-stimulant medications such as atomoxetine. In Singapore, the only stimulant medication available is methylphenidate, which is classified as a controlled drug. While most of the discussion will focus on medications available in Singapore, information on other available medication options will be presented in the summary tables.

When considering medication for the treatment of ADHD, there are several factors to consider including the age of the patient, severity of the ADHD symptoms and resultant impairment, co-morbid conditions and safety issues.

## 5.1 Methylphenidate

Among the various types of stimulant medication, there is insufficient evidence to suggest that any particular one is superior to methylphenidate.[148] Methylphenidate is available in both short-acting and long-acting/extended-release preparations. Short-acting methylphenidate lasts about 4 hours whereas long-acting/extended-release preparations can last 8-12 hours. Methylphenidate has been consistently reported to be effective in reducing the core symptoms of ADHD in several meta-analyses.[80,149] Randomised prospective long term studies have shown that methylphenidate continues to be effective in treating these symptoms over 1 to 5 years, although methodological limitations exist for many of these trials.[81,150-153] In a meta-analysis of 32 double-blind, placebo-controlled trials in youths (aged 6–18 years) with ADHD, stimulant medication was found to be more effective than non-stimulant medications.[154]

**A** When medication is considered for the treatment of attention deficit hyperactivity disorder, methylphenidate should be considered first.

**Grade A, Level 1+**

**B** Methylphenidate may be used for long term treatment of attention deficit hyperactivity disorder symptoms, although the benefits of treatment should be reviewed regularly.

**Grade B, Level 1+**

### 5.1.1 Safety and tolerability

Most of the side effects of methylphenidate are generally mild. In children, abdominal pain, insomnia, tachycardia, irritability, loss of appetite and headache may occur more frequently than in adults.[149] The incidence of adverse events increases with dosage both for short-acting and extended-release methylphenidate preparations.[155,156]

A drug holiday is a medication-free period during its systematic use. Methylphenidate omission during weekends or school holidays is a common way to establish a drug holiday. A small randomised controlled trial suggested that weekend holiday use during methylphenidate administration reduced the side effects of insomnia and appetite suppression without a significant increase in symptoms.[157] Weekend and

"drug holidays" can limit some adverse effects (e.g. appetite suppression, abdominal pain, headache, insomnia, irritability and tics).[158]

**B** Drug holidays during treatment with methylphenidate may be considered in order to limit adverse effects. Attention deficit hyperactivity disorder symptoms and impairment during the non-medication days should be monitored.

**Grade B, Level 1+**

The important side effects of methylphenidate which will be discussed here include growth suppression and cardiovascular safety.[159]

**Growth suppression**

There are positive and negative studies about the effect of methylphenidate on the growth of children with ADHD who were treated. Longitudinal studies reporting a positive effect showed that the reduction in both height and weight gain occurred mainly during the initial period of treatment (6 months to 3 years), although it is not clear if subsequent rebound growth would occur.[160-164]

Stimulant medication may also be associated with reduced growth velocity during the initial years.[165] One case-control study involving Chinese school-aged children showed a small deceleration of height velocity, and the magnitude of height deficit to be related to the duration of treatment with methylphenidate, but no significant effect on their weight.[166] Another longitudinal case-control study did not find medication to have an effect on growth 10 years later.[167] While two longitudinal studies suggested that a higher dose of methylphenidate was associated with reduced height and/or weight gain,[163,168] drug holidays did not appear to reduce its effect on physical growth.[168,169] Another longitudinal study found medication dose to be inversely correlated with the height velocity from baseline to 14.00-16 years of age.[170]

**A** The height, weight and body-mass-index (BMI) of children receiving treatment with methylphenidate should be regularly monitored.

**Grade A, Level 1++**

**D** The height, weight and body-mass-index (BMI) of children receiving treatment with methylphenidate should be monitored every 6 months. If

there is concern about slowing of growth rate, the need for continued medication use should be reviewed and jointly decided with parents, and there may be a need to evaluate for other medical reasons explaining this.

**Grade D, Level 4**

**B** During treatment with methylphenidate, start at a low dose and slowly titrate upwards according to the child's response, or adjust the timing of medication, to minimise short-term adverse effects.

**Grade B, Level 1+**

### Cardiovascular effects

A review which examined seven population-based observational studies involving children and adolescents found that six of these studies, which involved over 1.5 million person-years in total, did not show an association between stimulant use and adverse cardiovascular outcomes including deaths.[171] The last study was a case–control study which matched 564 cases of sudden death among youth 7 to 19 years old, with deceased passenger victims in motor vehicle accidents, and found stimulant use to be associated with increased odds of sudden death.[172]

Elevated heart rates and blood pressures may be associated with the use of methylphenidate.[173,174] Most of these elevated readings are sporadic and resolve during ongoing treatment,[175] although some studies suggest that the effects can be persistent.[176] How these small elevations in blood pressure and heart rate may affect individuals with pre-existing heart disease is not clear at present. The use of routine screening electrocardiogram (ECG) in asymptomatic individuals before starting treatment with stimulant medication would not prevent sudden death, and is not cost-effective.[177] The FDA recommends that stimulant products and atomoxetine should generally not be used in patients with serious heart problems, or for whom an increase in blood pressure or heart rate would be problematic.

**C** A careful personal and family history of cardiovascular disease should be taken before starting medication treatment for attention deficit hyperactivity disorder. Children with pre-existing cardiac problems should be referred to a cardiologist for evaluation before treatment with methylphenidate or atomoxetine is initiated.

**Grade C, Level 2+**

## 5.1.2 Treatment in the presence of comorbidities

### Tic disorder

One meta-analysis of treatment involving children with ADHD and co-morbid tics found that methylphenidate did not worsen tics.[178] While the Cochrane review supported this finding, it noted that there were a few individuals whose tics were worsened with stimulant medication.[179]

**A** Methylphenidate may be used to treat attention deficit hyperactivity disorder in children with comorbid tic disorder but treatment should be stopped if the tics worsen following treatment.

**Grade A, Level 1+**

### Oppositional defiant disorder/Conduct disorder

Oppositional defiant disorder or conduct disorder are disruptive behavioural disorders which can co-exist with ADHD. The MTA study found that methylphenidate is beneficial when there is a co-morbid disruptive behaviour disorder.[22]

**B** The use of methylphenidate should be considered when treating attention deficit hyperactivity disorder in the presence of co-morbid disruptive behavioural disorder.

**Grade B, Level 1+**

### Substance use disorder

The uses of the immediate-release preparation of methylphenidate and substance misuse are risk factors for drug diversion (giving, selling or trading their medication).[180,181] A review of two randomised controlled trials using osmotic-release methylphenidate concluded that it can be safely used in adolescents with a substance use disorder.[182] The presence of strict prescription control regulation helps to reduce stimulant abuse and diversion of medications.[183]

**B** The use of an extended-release methylphenidate instead of immediate-release methylphenidate should be considered if there is concern about medication abuse. Medication use by these patients should be carefully monitored.

**Grade B, Level 1+**

**Autistic spectrum disorder**

As previously discussed, DSM-V now permits the co-diagnosis of ADHD with autistic spectrum disorder. A meta-analysis of four double-blind, randomised, placebo-controlled trials examining the efficacy of methylphenidate for treating ADHD symptoms in children with autistic spectrum disorder showed methylphenidate to be effective for treating ADHD symptoms.[184] However, methylphenidate has been associated with more adverse events in children with ASD, particularly among the pre-school aged children.[184,185]

**A** Methylphenidate may be considered for the treatment of attention deficit hyperactivity disorder in individuals who have also been diagnosed with autistic spectrum disorder. Care should be taken to watch for side effects.

**Grade A, Level 1+**

### 5.1.3 Drug interactions with methylphenidate

Drugs with significant interactions with methylphenidate are summarized in Annex 4.

## 5.2 Atomoxetine

Atomoxetine is a non-stimulant medication for the treatment of ADHD. The effects of atomoxetine may not be apparent for up to 4 weeks or even later. Unlike stimulant medication, atomoxetine requires regular dosing and relies on longer-acting effects of the medication. Meta-analyses reviewing trials of head-to-head comparison between methylphenidate and atomoxetine showed that methylphenidate resulted in greater improvement within the first 2 weeks, although both had comparable short-term (6-week) efficacy.[186-189] One meta-analysis found that atomoxetine is effective in the treatment of ADHD in children and young people in the longer term (at least two years) but with a smaller effect size than methylphenidate.[190, 191]

The cost of atomoxetine is higher than methylphenidate in Singapore.

**A** Atomoxetine may be used for the treatment of attention deficit hyperactivity disorder symptoms when there is increased risk with methylphenidate use (e.g. high risk of abuse or diversion).

**Grade A, Level 1+**

### 5.2.1 Safety and tolerability

Because of the continuous action of atomoxetine, a drug holiday is not an option for reducing or preventing adverse effects.

One review found that atomoxetine resulted in higher rates of vomiting and drowsiness, similar rates of nausea and anorexia, and lower rates of insomnia than stimulants.[192,193] One such double-blind randomised controlled trial comparing atomoxetine with short-acting methylphenidate which reported this finding had involved Asian subjects.[194] One of the commonest adverse effects associated with atomoxetine use for 3 years and more includes suicidal ideation.[195]

One meta-analysis examining the effect of atomoxetine on growth among those aged 6-16 who were treated for at least 2 years found that while there was minimal effect on growth on those in the lowest quartile, those who were in the highest quartile for height and weight showed a decrease.[196] Similarly, another open-label study of 61 children who received atomoxetine and were followed up for 5 years found that those who were larger than average at the start of treatment showed decreases both for weight and height.[197]

Short-term trials have suggested that atomoxetine can increase heart rate and blood pressure.[198-200] Several reviews of longer-term trials lasting up to 3 years reported similar findings although the confounding effect of increased age (which is associated with increased blood pressure) has not been examined.[195, 201]

**A** During treatment with atomoxetine, there should be periodic monitoring of growth (height and weight) and mental state (suicidal thinking). If there is concern about slowing of growth rate, the need for continued medication use should be reviewed and jointly decided with parents, and there may be a need to evaluate for other medical reasons explaining this.

**Grade A, Level 1++**

**D** The height, weight and body-mass-index (BMI) of children receiving treatment with atomoxetine should be monitored every 6 months.

**Grade D, Level 4**

## 5.2.2 Treatment in the presence of comorbidities

### Tic disorder

One meta-analysis found that atomoxetine and alpha-2 agonists improved both ADHD and tic symptoms.[178]

### Oppositional defiant disorder/Conduct disorder

One 9-week double-blind randomised controlled trial involving children and adolescents aged 6-17 years with comorbid ADHD and ODD or CD reported atomoxetine to be beneficial in improving behavioural outcomes.[202] However, longer term effects of atomoxetine treatment are not known.

### Substance use disorder

Because of concerns over the potential for abuse with stimulant medication, atomoxetine or bupropion may be preferred in individuals with active substance abuse disorders. A placebo-controlled trial involving 70 adolescents with ADHD and non-nicotine substance use disorder who were randomised to receive 12 weeks of atomoxetine or placebo, combined with motivational interviewing and cognitive- behavioural therapy did not find any difference in ADHD symptoms or substance use between both groups.[203]

**B** Atomoxetine may be used as first line treatment when there is comorbid attention deficit hyperactivity disorder and tic disorder.

**Grade B, Level 1+**

### Autistic spectrum disorder

A meta-analysis found two double-blind, randomised, placebo-controlled trials examining the efficacy of atomoxetine for treating ADHD symptoms in children with autistic spectrum disorder. Atomoxetine appears to be beneficial but results in increased rates of side effects particularly of nausea, decreased appetite, and early morning awakening.[184]

## 5.3 Other medications

There are other classes of medications which have been investigated for the treatment of ADHD. These medications are either not available in Singapore, or are not used as first-line options for treatment.

### 5.3.1 Anti-psychotic medication

Aggressive behaviour may be associated with ADHD and treating ADHD with stimulant medication can be helpful in reducing aggressive behaviour.[204] Anti-psychotic medication has been used to target aggressive behaviour rather than ADHD symptoms per se. The most studied anti-psychotic medication is risperidone. There is some evidence that risperidone may reduce aggression in children who are disruptive with a low IQ.[205-207] One placebo-controlled pilot study reported a combination of risperidone and stimulant medication to be moderately efficacious and well-tolerated when used to treat aggression with a primary diagnosis of ADHD.[208,209] Risperidone however is associated with side effects such as include somnolence, weight gain, metabolic problems, and extrapyramidal side effects.

### 5.3.2 Alpha-adrenergic agonists

The main alpha-2 agonists used to treat ADHD are clonidine and guanfacine. One 16-week, randomised, double-blind, placebo-controlled clinical trial conducted in 122 children aged 7 to 12 concluded that methylphenidate was a better option when considering both efficacy and tolerability.[210] A review of two large controlled trials concluded that guanfacine was effective in reducing ADHD symptoms.[211] Some common side effects associated with clonidine and guanfacine include drowsiness and reductions in heart rate and blood pressure.[212-214]

### 5.3.3 Antidepressants

Bupropion is used for treating depression and smoking cessation. Its main effects include increasing noradrenergic and dopaminergic activity. In a 6-week randomised double-blind study involving 44 patients aged 6-17 diagnosed with ADHD, there was no difference in outcome between those who received bupropion and those who received methylphenidate.[215]

However, more studies will need to be done for bupropion, as an earlier study suggested that it could be associated with the onset of tics and extreme irritability in children.[216]

Clinical trials examining tricyclic antidepressants were generally old, and they improve hyperactive-impulsive symptoms more than inattentive symptoms.[217,218] One review found methylphenidate to be superior to imipramine in treating ADHD.[219] One case series of 14 children with inadequate response to stimulant medication reported improvement following treatment with reboxetine.[220] Another open-label study involving 17 adolescents found duloxetine to be effective in all domains of ADHD symptoms, with the effect seen from week 4 onwards.[221]

## 5.4 Medication combination for treating ADHD symptoms

More research addressing the efficacy and safety of using combination of medications in the control of ADHD symptoms is needed.

A small pilot study examining the strategy of augmentating atomoxetine with methylphenidate found increased treatment effect after one week but not by the 6th week, when compared with atomoxetine plus placebo. The combination of atomoxetine and methylphenidate appeared to be safe and did not result in more adverse events compared to the atomoxetine plus placebo group.[222]

A recent review on the studies and case reports on the use of a combination of stimulant medication with atomoxetine concluded that there was only limited evidence to support its use.[223]

**C** The combination of methylphenidate and atomoxetine should not be used for the treatment of attention deficit hyperactivity disorder symptoms.

**Grade C, Level 2+**

Several short-term double-blind placebo-controlled trials examined the efficacy of combination of clonidine and methylphenidate in treating children and adolescents with ADHD who did not respond adequately to stimulant medication previously. The combination of methylphenidate plus clonidine improved ADHD symptom control and was safe.[224, 225] However, evidence of long term efficacy is lacking.

## 5.5 Treatment Adherence

Treatment non-adherence to stimulant medication can be as high as 64%.[226] Parental factors are important in influencing treatment adherence, especially their concerns about the negative effects of treatment.[227-230] Older teenagers may make their own decisions about stopping medication.[231]

**A** To improve treatment adherence, treatment should be individualised for each patient with attention deficit hyperactivity disorder, and the parents' and their child's preferences should be considered.

**Grade A, Level 1+**

## 5.6 Use of medication in pre-schoolers

Methylphenidate is effective in reducing core ADHD symptoms over a 10-month treatment period, and in improving short-term function among pre-schoolers, although the improvement in ADHD symptoms appear to be less than that observed in older children.[232-234] The use of methylphenidate in pre-schoolers is associated with higher rates of adverse effects including social withdrawal, irritability and crying, and reduced growth rates.[235, 236]

Atomoxetine has been used to treat 5- and 6-year old children with ADHD in a double-blind placebo-controlled trial. There was improvement in reported ADHD symptoms and side effects were experienced by up to one third of the children.

Because of lower effect size and higher incidence of side effects, most guidelines recommend the use of evidence-based psychosocial interventions such as parent training (see next section) as the first-line treatment.

**A** The use of methylphenidate or atomoxetine in pre-schoolers should be considered only if psychosocial interventions have failed. Care should be taken to regularly assess response and monitor for side effects, so as to decide if medication should continue to be administered.

**Grade A, Level 1++**

## 6 Cost-effectiveness issues

A recent review of economic evaluation studies to determine the cost-effectiveness of pharmacotherapy for ADHD concluded that among children and adolescents with ADHD, there was consistent evidence that pharmacotherapies are cost-effective compared with no treatment or behavioural therapy; however there was insufficient data to examine the relative cost effectiveness of different pharmacological agents.[237]

Another systematic review found medical management to be superior to non-medical management and no significant differences between the various drugs in terms of efficacy or adverse effects were found.[238] Comparing the treatment options of medication management, behavioural treatment, or combination of the two, medication management was more cost-effective.[239]

**A** Although medication is a cost-effective treatment for attention deficit hyperactivity disorder (ADHD), treatment for ADHD should be individualised and other factors (e.g. presence of co-morbidity) should be considered before initiating medications.

**Grade A, Level 1++**

# 7 Clinical quality improvement

This CPG for ADHD in children and adolescents was formulated to assist local practitioners in the areas of diagnosis and intervention. In Singapore, this is a condition which used to be diagnosed and treated mainly by psychiatrists attending to child and adolescents, and paediatricians have more recently started attending to this group as well. At present, general practitioners are also gradually getting involved in the recognition and treatment of this condition.

The following clinical quality indicators in the areas help to provide an indication of the quality of care when diagnosing and treating young persons with ADHD. Clinicians should work towards achieving 100% for each clinical quality indicator.

1. A thorough history should be obtained from both parents and another adult (e.g. teachers) to establish the presence of symptoms in at least two settings, before diagnosing an individual with ADHD.

**Clinical Quality Indicator:** Percentage of newly-diagnosed cases of ADHD with history obtained from another adult other than parents

2. When treating a school-going child with ADHD, the clinician should educate teachers about the diagnosis and classroom behaviour management strategies, provided consent is obtained from parents.

**Clinical Quality Indicator:** Percentage of patients with communication with school teachers about classroom behaviour management strategies

3. Growth suppression is an adverse effect of concern to parents and clinicians should monitor this when using methylphenidate or atomoxetine to treat ADHD.

**Clinical Quality Indicator:** Percentage of patients treated with methylphenidate or atomoxetine who have their height, weight and BMI monitored every 6 months or visit, whichever is less frequent.

## Annex 1

**Differential diagnoses for ADHD**

*Psychiatric or developmental disorders*

- Disruptive Behaviour Disorder (Oppositional defiant disorder, Conduct disorder)
- Intellectual disability / borderline intellectual functioning
- Autism and Asperger's syndrome
- Anxiety disorders (including obsessive compulsive disorder)
- Alcohol and substance abuse, dependence or withdrawal
- Tic disorders (including Tourette's disorder)
- Specific development disorder (e.g. speech, language and learning difficulties)
- Mood disorder
- Schizophrenia
- Reactive attachment disorder

*Medical conditions*

- Medical problems (e.g. hyperthyroidism and epilepsy)
- Neurological conditions (e.g. head injury, epilepsy)
- Medication-related problems (e.g. anti-asthmatics, anticonvulsants, antihistamines, sympathomimetics and steroids)

*Psychosocial problems*

- Reactive attachment disorder
- Child abuse
- Parental/family conflict

Footnote: This list is not exhaustive

## Annex 2

**Questionnaires (or Rating Scales) to assess ADHD symptoms, and some online resources**

Rating Scales

1. The Conners' Rating Scales-Revised
   - Conners' Parent Rating Scale – Revised
   - Conners' Teacher Rating Scale – Revised
   - Conners-Wells' Adolescent Self Report Scales

2. ADHD Rating Scale-IV

Online resources

1. Society for the Promotion of ADHD Research and Knowledge (www.spark.org.sg)

2. American Academy of Child and Adolescent Psychiatry (www.aacap.org/cs/ADHD.ResourceCenter)

3. CADDRA Canadian ADD ADHD Research Association (www.caddra.ca)

4. National Institute of Mental Health (www.nimh.nih.gov)

## Annex 3a Medications used in ADHD – Onset, Duration of action, Initial Dose & FDA Max dose/day

**Medications Used in ADHD**[240-249]

| Generic Class/ Brand Name | Onset | Duration of action | Initial Dose | FDA Max dose/day |
|---|---|---|---|---|
| **Methylphenidate preparation** | | | | |
| **Short acting** | | | | |
| Ritalin (Methylphenidate) | 20 – 60 min | 2 – 4 hours | 5mg BD<br>5 – 10mg weekly titration | 60mg |
| **Intermediate acting** | | | | |
| Ritalin LA (Methylphenidate)<br>50% of dose released immediately; 50% delayed-release delivered gradually over prolonged period. | 20 – 60 min | 4 – 8 hours | 20mg OM<br>5 – 10mg weekly increment | 60mg |
| **Long acting** | | | | |
| Concerta (Methylphenidate)<br>22% of dose coated on outside of shell for immediate release and remaining 78% gradually released in controlled and timed fashion throughout the day. | 30 min – 2 hours | 8 – 12 hours | 18mg OM<br>18mg weekly titration | 72mg |
| **Selective norepinephrine reuptake inhibitor*** | | | | |
| Atomoxetine (Strattera) | Approximately 4 – 6 weeks | 24 hours | • Children & adolescent <70kg: 0.5mg/kg/day for 4 days; then 1mg/kg/day for 4 days; then 1.2mg/kg/day<br>• >70kg: 40mg OD for 4 days, increase to 80mg OD or may be evenly divided into 2 doses | Lesser of 1.4mg/kg or 100mg |
| **Antidepressants – Bupropion†** | | | | |
| Wellbutrin<br>Wellbutrin SR<br>Wellbutrin XL | | | 3mg/kg/day or 150mg/day | 6mg/kg/day or 300mg with no single dose >150mg |
| **Tricyclic antidepressant†** | | | | |
| Imipramine | | | 1mg/kg/day | 4mg/kg/day or 200mg |
| Nortriptyline | | | 0.5mg/kg/day | 2mg/kg/day or 100mg |

Note:
* **Long term studies (>12 months) available**
† **FDA not approved**

## Annex 3b Medications used in ADHD – Common side effects

| Medications | Comments | Common side effects |
|---|---|---|
| **Stimulants** | | |
| Short acting methylphenidate (e.g. Ritalin) | • Short acting stimulants often used as initial treatment in small children (<16kg) but have disadvantage of BD to TDS dosing to control symptoms throughout day.<br>• Give doses at least 4 hours apart.<br>• Dex-methylphenidate: conversion form methylphenidate; initiate at half the total daily dose of racemic methylphenidate. | • Insomnia<br>• Headache<br>• Decreased appetite<br>• Restlessness<br>• Abdominal pain<br>• Increased heart rate |
| Intermediate acting methylphenidate (e.g. Ritalin LA) | • Longer acting stimulants offer greater convenience, confidentiality and compliance with single daily dosing but may have greater problematic on evening appetite and sleep.<br>• In general, switching to long-acting formulation dose is equivalent to previous total daily dose.<br>• Ritalin LA capsules may be opened and sprinkled on soft foods. | |
| Long acting methylphenidate (e.g. Concerta) | • Swallow whole with liquids.<br>• Non-absorbable tablet shells may be seen in stools. | |
| **Non-stimulants** | | |
| Selective norepinephrine reuptake inhibitor (e.g. Atomoxetine) | • The full effect may not be seen for up to 4 weeks on a given target dose.<br>• Capsule should not be open as atomoxetine is an ocular and mucous membrane irritant.<br>• May be discontinued without tapering the dose. | • Decreased appetite<br>• Dyspepsia<br>• Dizziness<br>• Fatigue<br>• Sedation<br>• Nausea<br>• Emesis<br>• Mood swings<br>• Growth delay<br>• Increased heart rate or blood pressure, urinary retention, rare severe liver injury. |
| Bupropion | • Lower seizure threshold; contraindicated if current seizure disorder.<br>• Usually given in divided dose, BD for children, TDS for adolescents, for both safety and effectiveness.<br>• To reduce seizure risk, space regular tablets at least 4 – 6 hours apart and sustained released tablets 8 hours apart.<br>• Contraindicated in bulimic patients, head trauma & epilepsy. | • Insomnia<br>• Irritability<br>• Drug-induced seizures (with dose >6mg/kg) |
| Tricyclic antidepressants (e.g. imipramine, nortriptyline) | • Usually reserved for older children and adolescent not responding to stimulants.<br>• Obtain baseline ECG before starting imipramine and nortriptyline. | • Dry mouth<br>• Urinary retention<br>• Headache |

## Annex 4 Significant drug-drug interactions of methyphenidate

Methylphenidate is very effective in the treatment of ADHD. Fortunately, very few clinically relevant drug-drug interactions exist with this medication. Clinically important drug interactions involving stimulant medications are outlined **below**. The use of stimulant medication with a monoamine oxidase inhibitor (MAOI) is contraindicated.[250]

| Drug classes | Interaction rating* | Proposed mechanism | Pharmacodynamic effect(s) | Pharmacokinetic effect(s) | Recommendation |
|---|---|---|---|---|---|
| MAOIs<br>- Isocarboxid<br>- Phenelzine<br>- Trancylcypromine | A/C | Interferes with biogenic amine metabolism; excessive adrenergic stimulation | Hyperpyrexia, hypertension, cerebral haemorrhage, arrhythmias, seizures | None | Avoid |
| Neuroleptics<br>- Haloperidol<br>- Chlorpromazine<br>- Prochlorperazine<br>- Trifluoperazine | A/C | Stimulants increase release of dopamine antagonising neuroleptic's pharmacodynamic effects | Antagonize neuroleptic effects (breakthrough psychotic events) | None | Careful dose titration |
| SSRIs<br>- Fluoxetine<br>- Fluvoxamine<br>- Paroxetine<br>- Sertraline | B/C | Stimulants initiate release of serotonin; amphetamine is partially metabolized by CYP2D6 and selected SSRIs inhibit CYP2D6 activity. | Increased serotonin receptor activity due to decreased reuptake; serotonin syndrome (i.e. hyperpyrexia, change in mental status, hypertension and tachycardia); amphetamine excess (increased heart rate, blood pressure and hyperactivity) | Possible increase of amphetamine serum concentration | Careful dose titration |
| TCAs<br>- Amitriptyline<br>- Desipramine<br>- Imipramine<br>- Nortriptyline | B | Stimulants may inhibit metabolism of imipramine; stimulants may increase the release of serotonin and TCAs prevent neuronal reuptake. | Serotonin syndrome | Possible increased TCA serum concentration | Careful dose titration |

Note:
*Rating of drug interaction potential
**A = well/ fairly well documented from clinical trials**
**B = scattered case reports and conflicting data**
**C = theoretical possibility**

## Annex 5

**Guidelines for communications between physicians and schools**

In the course of treating school-aged children with ADHD, physicians may need to communicate with schools for various reasons. This may include sharing the child's diagnosis and proposed intervention plans, or obtaining information from school personnel about the child's needs and behaviour in school.

To facilitate such communication, physicians are encouraged to refer to the following guidelines when initiating contact with schools:

- Obtain written consent from the child's parents before making contact with the school about individual children.
- Direct the initial contact with the school to the Principal. This is best done in writing, e.g. through an email or a letter. A sample letter is enclosed in the next page. Contact details of all mainstream schools in Singapore can be found at http://app.sis.moe.gov.sg/schinfo/.
- Following the initial contact, the Principal will identify the appropriate school personnel to liaise directly with the physicians. To facilitate the two-way communication, physicians are encouraged to include their contact details (email address and/or phone) in the letter.

*(Date)*

*(Name of Principal of School)*
*(Name of School)*
*(Address of School)*

Dear Principal,

I am currently seeing _____*(Child's Name and Birth Certificate No.)*_____ for assessment / treatment* *delete where applicable* of attention deficit hyperactivity disorder (ADHD). I have obtained parental consent to work with the school to support the abovementioned child's needs.

***Please tick where applicable:***

☐ I would like to request for information about the child's behaviour in the school setting from key school personnel who are familiar with the child. This information is required for my assessment and treatment of the child's condition.
I have enclosed a questionnaire that should be completed by a teacher and/or Allied Educator who has worked closely with the child for at least six months. Please complete the questionnaire and return it to the following address by _____*(date)*:
_____*(return address)*.

☐ I have assessed the abovementioned child on _____ *[Date(s) of assessment(s)]*.
You will find enclosed a diagnostic report for details of the child's diagnosis and recommendations for support. Please work with the relevant school staff to support the child's learning and behaviour in the school. You may also consult your school's psychologist, if necessary.

Sincerely,

_____
*(Name and Signature of Physician)*

_____
*(Email Address/Contact No.)*

## References


1 Polanczyk G, de Lima MS, Horta BL, Biederman J, Rohde LA. The worldwide prevalence of ADHD: a systematic review and metaregression analysis. Am J Psychiatry. 2007 Jun;164(6):942-8.

2 Woo BS, Ng TP, Fung DS, Chan YH, Lee YP, Koh JB, et al. Emotional and behavioural problems in Singaporean children based on parent, teacher and child reports. Singapore Med J. 2007 Dec;48(12):1100-6.

3 Faraone SV, Biederman J, Mick E. The age-dependent decline of attention deficit hyperactivity disorder: a meta-analysis of follow-up studies. Psychol Med. 2006;36(2):159-65.

4 Willcutt EG, Nigg JT, Pennington BF, Solanto MV, Rohde LA, Tannock R, et al. Validity of DSM-IV attention deficit/hyperactivity disorder symptom dimensions and subtypes. J Abnorm Psychol. 2012 Nov;121(4):991-1010.

5 Polanczyk G, Caspi A, Houts R, Kollins SH, Rohde LA, Moffitt TE. Implications of extending the ADHD age-of-onset criterion to age 12: results from a prospectively studied birth cohort. J Am Acad Child Adolesc Psychiatry. 2010 Mar;49(3):210-6.

6 Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry. 2005 Jun;62(6):593-602.

7 Biederman J, Mick E, Spencer T, Surman C, Hammerness P, Doyle R, et al. An open-label trial of OROS methylphenidate in adults with late-onset ADHD. CNS Spectr. 2006 May;11(5):390-6.

8 Barkley RA, Fischer M, Edelbrock CS, Smallish L. The adolescent outcome of hyperactive children diagnosed by research criteria: I. An 8-year prospective follow-up study. J Am Acad Child Adolesc Psychiatry. 1990 Jul;29(4):546-57.

9 Hoza B, Gerdes AC, Hinshaw SP, Arnold LE, Pelham WE, Jr., Molina BS, et al. Self-perceptions of competence in children with ADHD and comparison children. J Consult Clin Psychol. 2004 Jun;72(3):382-91.

10 Sayal K, Goodman R. Do parental reports of child hyperkinetic disorder symptoms at school predict teacher ratings? Eur Child Adolesc Psychiatry. 2009;18(6):336-44.

11 Sayal K, Taylor E. Parent ratings of school behaviour in children at risk of attention deficit/hyperactivity disorder. Acta Psychiatr Scand. 2005;111(6):460-5.

12 de Nijs P, Ferdinand R, de Bruin E, Dekker M, van Duijn C, Verhulst D. Attention-deficit/hyperactivity disorder (ADHD): parents' judgment about school, teachers' judgment about home. Eur Child Adolesc Psychiatry. 2004;13(5):315-20.

13 Mitsis E, McKay K, Schulz K, Newcorn J, Halperin J. Parent-teacher concordance for DSM-IV attention-deficit/hyperactivity disorder in a clinic-referred sample. Eur Child Adolesc Psychiatry. 2000;39(3):308-13.

14 Thapar A, Cooper M, Eyre O, Langley K. What have we learnt about the causes of ADHD? J Child Psychol Psychiatry. 2013 Jan;54(1):3-16.

15 Keenan K, Wakschlag LS. More than the terrible twos: the nature and severity of behavior problems in clinic-referred preschool children. J Abnorm Child Psychol. 2000 Feb;28(1):33-46.

16 Harvey EA, Arnold DH. ADHD symptom severity and diagnosis remains relatively stable over 6-year period following diagnosis in preschool. Evid Based Ment Health. 2013 Aug;16(3):63.

17 Lahey BB, Pelham WE, Stein MA, Loney J, Trapani C, Nugent K, et al. Validity of DSM-IV attention-deficit/hyperactivity disorder for younger children. J Am Acad Child Adolesc Psychiatry. 1998 Jul;37(7):695-702.

18 Willoughby MT, Pek J, Greenberg MT. Parent-reported Attention Deficit/Hyperactivity symptomatology in preschool-aged children: factor structure, developmental change, and early risk factors. J Abnorm Child Psychol. 2012 Nov;40(8):1301-12.

19 Lahey BB, Pelham WE, Loney J, Kipp H, Ehrhardt A, Lee SS, et al. Three-year predictive validity of DSM-IV attention deficit hyperactivity disorder in children diagnosed at 4-6 years of age. Am J Psychiatry. 2004 Nov;161(11):2014-20.

20 Biederman J, Newcorn J, Sprich S. Comorbidity of attention deficit hyperactivity disorder with conduct, depressive, anxiety, and other disorders. Am J Psychiatry. 1991 May;148(5):564-77.

21 A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. The MTA Cooperative Group. Multimodal Treatment Study of Children with ADHD. Arch Gen Psychiatry. 1999 Dec;56(12):1073-86.

22 Jensen PS, Hinshaw SP, Kraemer HC, Lenora N, Newcorn JH, Abikoff HB, et al. ADHD comorbidity findings from the MTA study: comparing comorbid subgroups. J Am Acad Child Adolesc Psychiatry. 2001 Feb;40(2):147-58.

23 Milberger S, Biederman J, Faraone SV, Murphy J, Tsuang MT. Attention deficit hyperactivity disorder and comorbid disorders: issues of overlapping symptoms. Am J Psychiatry. 1995 Dec;152(12):1793-9.

24 Yoshimasu K, Barbaresi WJ, Colligan RC, Killian JM, Voigt RG, Weaver AL, et al. Gender, attention-deficit/hyperactivity disorder, and reading disability in a population-based birth cohort. Pediatrics. 2010 Oct;126(4):e788-95.

25 Yoshimasu K, Barbaresi WJ, Colligan RC, Killian JM, Voigt RG, Weaver AL, et al. Written-language disorder among children with and without ADHD in a population-based birth cohort. Pediatrics. 2011 Sep;128(3):e605-12.

26 Gudjonsson GH, Sigurdsson JF, Sigfusdottir ID, Young S. An epidemiological study of ADHD symptoms among young persons and the relationship with cigarette smoking, alcohol consumption and illicit drug use. J Child Psychol Psychiatry. 2012 Mar;53(3):304-12.

27 van Emmerik-van Oortmerssen K, van de Glind G, van den Brink W, Smit F, Crunelle CL, Swets M, et al. Prevalence of attention-deficit hyperactivity disorder in substance use disorder patients: a meta-analysis and meta-regression analysis. Drug Alcohol Depend. 2012 Apr 1;122(1-2):11-9.

28 Silver LB. Attention deficit-hyperactivity disorder: is it a learning disability or a related disorder? J Learn Disabil. 1990 Aug-Sep;23(7):394-7.

29 Becker SP, Langberg JM, Vaughn AJ, Epstein JN. Clinical utility of the vanderbilt ADHD diagnostic parent rating scale comorbidity screening scales. J Dev Behav Pediatr. Apr;33(3):221-8.

30 Tuthill R. Hair lead levels related to children's classroom attention-deficit behavior. Arch Environ Health. 1996;52:214–20.

31 Weiss R, Stein M, Trommer B, Refetoff S. Attention-deficit hyperactivity disorder and thyroid function. J Pediatr. 1993;123:539-45.

32 Green M, Wong M, Atkins D, Taylor J, Feinleib M. Diagnosis of Attention-Deficit/ Hyperactivity Disorder. Rockville (MD): Agency for Health Care Policy and Research (AHCPR); 1999.

33 Monastra VJ, Lubar JF, Linden M, VanDeusen P, Green G, Wing W, et al. Assessing attention deficit hyperactivity disorder via quantitative electroencephalography: an initial validation study. Neuropsychology. 1999 Jul;13(3):424-33.

34 Clarke A, Barry R, McCarthy R, Selikowitz M. Excess beta activity in children with attention-deficit/hyperactivity disorder: An atypical electro-physiological group. . Psychiatry Research. 2001;103:205-18.

35 Lubar J. Discourse on the development of EEG diagnostics and biofeedback for attention-deficit/hyperactivity disorders. Biofeedback and Self Regulation. 1991;16:201-25.

36 Loo S, Makeig S. Attention-deficit/hyperactivity disorder: a research update. . Neurotherapeutics. 2012;9(3):569-87.

37 Arns M, Conners C, Kraemer H. A decade of EEG Theta/Beta Ratio Research in ADHD: a meta-analysis. J Atten Disord. 2013;17(5):374-83.

38 Boutros N, Fraenkel L, Feingold A. A four-step approach for developing diagnostic tests in psychiatry: EEG in ADHD as a test case. J Neuropsychiatry Clin Neurosci. 2005;17(4):455-64.

39 Weder N. Are we there yet? Electroencephalography as a diagnostic tool for attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry. 2013;52(11):1119-20.

40 Teicher M, Ito Y, Glod C, Barber N. Objective measurement of hyperactivity and attentional problems in ADHD. J Am Acad Child Adolesc Psychiatry. 1996;35:334-42.

41 Teicher M, Ito Y, Glod C, Wallace P. Quantitative assessment of fidgeting in attention-deficit hyperactivity disorder (ADHD). Am Acad Child Adolescence Psychiatry. 1993;9:42-3.

42 Martín-Martínez D, Casaseca-de-la-Higuera P, Alberola-López S, Andrés-de-Llano J, López-Villalobos J, Ardura-Fernández J, et al. Nonlinear analysis of actigraphic signals for the assessment of the attention-deficit/hyperactivity disorder. Med Eng Phys. 2012;34(9):1317-29.

43 Kam H, Lee K, Cho S, Shin Y, Park R. High-resolution actigraphic analysis of ADHD: a wide range of movement variability observation in three school courses - a pilot study. Healthc Inform Res 2011. 2011;17:19-37.

44 Dane A, Schachar R, Tannok R. Does actigraphy differentiate ADHD subtypes in a clinical research setting? J Am Acad Child Adolesc Psychiatry. 2000;39:752-60.

45 Teicher M, Glod C, Pahlavan K, Harper D, Magnus E, Wren F. Locomotor activity and the diagnosis of ADHD. Am Psychiatr Assoc Abstr. 1991;141:98.

46 MTA Cooperative. A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. Arch Gen Psychiatry. 1999;56(12):1073-86.

47 Waschbusch DA, Cunningham CE, Pelham WE, Rimas HL, Greiner AR, Gnagy EM, et al. A discrete choice conjoint experiment to evaluate parent preferences for treatment of young, medication naive children with ADHD. J Clin Child Adolesc Psychol. 2011;40(4):546-61.

48 National Institute for Health and Clinical Excellence. Attention deficit hyperactivity disorder: diagnosis and management of ADHD in children, young people and adults. Clinical Guideline 72. London: National Institute for Health and Clinical Excellence; 2008.

49 Hall C, Newell K, Taylor J, Sayal K, Swift K, Hollis C. Mind the gap' - mapping services for young people with ADHD transitioning from child to adult mental health services. BMC Psychiatry 2013;13:186.

50 Young S, Murphy C, Coghill D. Avoiding the 'twilight zone': recommendations for the transition of services from adolescence to adulthood for young people with ADHD. BMC Psychiatry. 2011;3(11):174.

51 Cheok C. Will to Fight: A Psychological Management Guide for National Service. Singapore: Angsana Books; 2012.

52 Lopez MA, Toprac MG, Crismon ML, Boemer C, Baumgartner J. A psychoeducational program for children with ADHD or depression and their families: results from the CMAP feasibility study. Community Ment Health J. 2005 Feb;41(1):51-66.

53 McCleary L, Ridley T. Parenting adolescents with ADHD: evaluation of a psychoeducation group. Patient Educ Couns 1999;38:3-10.

54 Sonuga-Barke EJ, Daley D, Thompson M, Laver-Bradbury C, Weeks A. Parent-based therapies for preschool attention-deficit/hyperactivity disorder: a randomized, controlled trial with a community sample. J Am Acad Child Adolesc Psychiatry. 2001 Apr;40(4):402-8.

55 Miranda A, Presentacion MJ, Soriano M. Effectiveness of a school-based multicomponent program for the treatment of children with ADHD. J Learn Disabil. 2002 Nov-Dec;35(6):546-62.

56 Monastra VJ. Overcoming the barriers to effective treatment for attention-deficit/hyperactivity disorder: a neuro-educational approach. Int J Psychophysiol. 2005 Oct;58(1):71-80.

57 Svanborg P, Thernlund G, Gustafsson PA, Hagglof B, Poole L, Kadesjo B. Efficacy and safety of atomoxetine as add-on to psychoeducation in the treatment of attention deficit/hyperactivity disorder: a randomized, double-blind, placebo-controlled study in stimulant-naive Swedish children and adolescents. Eur Child Adolesc Psychiatry. 2009 Apr;18(4):240-9.

58 Montoya A, Colom F, Ferrin M. Is psychoeducation for parents and teachers of children and adolescents with ADHD efficacious? A systematic literature review. Eur Psychiatry. 2011 Apr;26(3):166-75.

59 Fields SA, Hale LR. Psychoeducational groups for youth attention-deficit hyperactivity disorder: a family medicine pilot project. Ment Health Fam Med. 2011 Sep;8(3):157-65.

60 O'Leary KD, Pelham WE, Rosenbaum A, Price GH. Behavioral treatment of hyperkinetic children. An experimental evaluation of its usefulness. Clin Pediatr (Phila). 1976 Jun;15(6):510-5.

61 Johnston C, Hommersen P, Seipp C. Acceptability of behavioral and pharmacological treatments for attention-deficit/hyperactivity disorder: relations to child and parent characteristics. Behav Ther 2008;39:22-32.

62 Pelham WE, Jr., Wheeler T, Chronis A. Empirically supported psychosocial treatments for attention deficit hyperactivity disorder. J Clin Child Psychol. 1998 Jun;27(2):190-205.

63 Pelham W, Fabiano G. Evidence-based psychosocial treatments for attention-deficit/hyperactivity disorder. J Clin Child Adolesc Psychol 2008;37:184-214.

64 Yamashita Y, Mukasa A, Anai C, Honda Y, Kunisaki C, Koutaki J, et al. Summer treatment program for children with attention deficit hyperactivity disorder: Japanese experience in 5 years. Brain Dev. 2011 Mar;33(3):260-7.

65 Hantson J, Wang PP, Grizenko-Vida M, Ter-Stepanian M, Harvey W, Joober R, et al. Effectiveness of a therapeutic summer camp for children with ADHD: Phase I Clinical Intervention Trial. J Atten Disord. 2012 Oct;16(7):610-7.

66 Johnston C, Mash EJ. Families of children with attention-deficit/hyperactivity disorder: review and recommendations for future research. Clin Child Fam Psychol Rev. 2001 Sep;4(3):183-207.

67 Jacobvitz D, Sroufe LA. The early caregiver-child relationship and attention-deficit disorder with hyperactivity in kindergarten: a prospective study. Child Dev. 1987 Dec;58(6):1496-504.

68 Modesto-Lowe V, Danforth JS, Brooks D. ADHD: does parenting style matter? Clin Pediatr (Phila). 2008 Nov;47(9):865-72.

69 Eyberg SM, Nelson MM, Boggs SR. Evidence-based psychosocial treatments for children and adolescents with disruptive behavior. J Clin Child Adolesc Psychol. 2008 Jan;37(1):215-37.

70 Charach A, Dashti B, Carson P, Booker L, Lim CG, Lillie E, et al. Effectiveness of Treatment in At-Risk Preschoolers; Long-Term Effectiveness in All Ages; and Variability in Prevalence, Diagnosis, and Treatment. Comparative Effectiveness Reviews. 2011 Oct Preschoolers; Long-Term Effectiveness in All Ages; and Variability in Prevalence, Diagnosis, and Treatment;44.

71 Charach A, Carson P, Fox S, Ali MU, Beckett J, Lim CG. Interventions for preschool children at high risk for ADHD: a comparative effectiveness review. Pediatrics. 2013 May;131(5):e1584-604.

72 Edwards RT, Ceilleachair A, Bywater T, Hughes DA, Hutchings J. Parenting programme for parents of children at risk of developing conduct disorder: cost effectiveness analysis. BMJ. 2007 Mar 31;334(7595):682.

73 Hanisch C, Freund-Braier I, Hautmann C, Janen N, Pluck J, Brix G, et al. Detecting effects of the indicated prevention Programme for Externalizing Problem behaviour (PEP) on child symptoms, parenting, and parental quality of life in a randomized controlled trial. Behav Cogn Psychother. 2010 Jan;38(1):95-112.

74 Zwi M, Jones H, Thorgaard C, York A, Dennis JA. Parent training interventions for Attention Deficit Hyperactivity Disorder (ADHD) in children aged 5 to 18 years. Cochrane Database Syst Rev. 2011(12):CD003018.

75 Kee C, Leong L, Teo J. Parenting behaviour and parenting sense of competence in parents with attention deficit hyperactivity disorder children. Annals, Academy of Medicine. 2004;33:S95-6.

76 Chronis AM, Jones HA, Raggi VL. Evidence-based psychosocial treatments for children and adolescents with attention-deficit/hyperactivity disorder. Clin Psychol Rev. 2006 Aug;26(4):486-502.

77 Laforett DR, Murray DW, Kollins SH. Psychosocial treatments for preschool-aged children with Attention-Deficit Hyperactivity Disorder. Dev Disabil Res Rev. 2008;14(4):300-10.

78 Barbaresi WJ, Katusic SK, Colligan RC, Weaver AL, Jacobsen SJ. Long-term school outcomes for children with attention-deficit/hyperactivity disorder: a population-based perspective. J Dev Behav Pediatr. 2007 Aug;28(4):265-73.

79 Frazier TW, Youngstrom EA, Glutting JJ, Watkins MW. ADHD and achievement: meta-analysis of the child, adolescent, and adult literatures and a concomitant study with college students. J Learn Disabil. 2007 Jan-Feb;40(1):49-65.

80 Van der Oord S, Prins PJ, Oosterlaan J, Emmelkamp PM. Efficacy of methylphenidate, psychosocial treatments and their combination in school-aged children with ADHD: a meta-analysis. Clin Psychol Rev. 2008 Jun;28(5):783-800.

81 National Institute of Mental Health Multimodal Treatment Study of ADHD follow-up: 24-month outcomes of treatment strategies for attention-deficit/hyperactivity disorder. Pediatrics. 2004 Apr;113(4):754-61.

82 Volpe RJ, DuPaul GJ, Jitendra AK, Tresco KE. Consultation-based academic interventions for children with Attention Deficit Hyperactivity Disorder: Effects on reading and mathematics outcomes at 1-year follow-up. School Psychology Review. 2009;38:5-13.

83 Jitendra AK, DuPaul GJ, Tresco KE, Vile-Junod RE, Lutz JG, Cleary KS, et al. Consultation-based academic intervention for children with Attention Deficit Hyperactivity Disorder: School functioning outcomes. School Psychology Review. 2007;36:217-36.

84 DuPaul GJ, Jitendra AK, Volpe RJ, Tresco KE, Lutz JG, Vile Junod RE, et al. Consultation-based academic interventions for children with ADHD: effects on reading and mathematics achievement. J Abnorm Child Psychol. 2006 Oct;34(5):635-48.

85 Reid R, Maag JW. Functional assessment: A method for developing classroom-based accommodations and interventions for children with ADHD. Reading & Writing Quarterly. 1998;14:9-42.

86 Brock SE, Jimerson SR, Hansen RL. Identifying, Assessing, and Treating ADHD in School2009.

87 Pariseau ME, Fabiano GA, Massetti GM, Hart KC, Pelham WE. Extended time on academic assignments: Does increased time lead to improved performance for children with attention-deficit/hyperactivity disorder? School Psychology Quarterly. 2010;25:236-48.

88 Lewandowskil LJ, Lovett BJ, Parolin R, Gordon M, Codding RS. Extended time accommodations and the mathematics performance of students with and without ADHD. Journal of Psychoeducational Assessment. 2007;25:17-28.

89 Elliott SN, Kratochwill TR, McKevitt BC, Malecki CK. The effects and perceived consequences of testing accommodations on math and science performance assessments. School Psychology Quarterly. 2009;24:224-39.

90 Scultz BK, Storer J, Watabe Y, Sadler J, Evans SW. School-based treatment of attention-deficit/hyperactivity disorder. Psychology in the Schools. 2011;48:254-62.

91 DuPaul GJ, Ervin RA, Hook CL, McGoey KE. Peer tutoring for children with attention deficit hyperactivity disorder: effects on classroom behavior and academic performance. J Appl Behav Anal. 1998 Winter;31(4):579-92.

92 Pfiffner LJ, Barkley RA, DuPaul GJ. Treatment of ADHD in school settings. Attention-deficit hyperactivity disorder: A handbook for diagnosis and treatment. (3rd ed.) New York, NY: Guilford Press; 2006.

93 Locke WR, Fuchs LS. Effects of peer-mediated reading instruction on the on-task behavior and social interaction of children with behavior disorders. Journal of Emotional and Behavioural Disorders. 1995;3:92-9.

94 Klingberg T, Fernell E, Olesen PJ, Johnson M, Gustafsson P, Dahlstrom K, et al. Computerized training of working memory in children with ADHD--a randomized, controlled trial. J Am Acad Child Adolesc Psychiatry. 2005 Feb;44(2):177-86.

95 Holmes J, Gathercole S, Place M, Dunning D, Hilyon K, Elliot J. Working memory deficits can be overcome: Impacts of training and medication on working memory in children with ADHD. Applied Cognitive Psychology. 2009;24:827-36.

96 Clarfield J, Stoner G. Research brief: The effects of computerized reading instruction on the academic performance of students identified with ADHD. School Psychology Review. 2005;34:246-54.

97 Mautone JA, DuPaul GJ, Jitendra AK. The effects of computer-assisted instruction on the mathematics performance and classroom behavior of children with ADHD. J Atten Disord. 2005 Aug;9(1):301-12.

98 Storebo OJ, Skoog M, Damm D, Thomsen PH, Simonsen E, Gluud C. Social skills training for Attention Deficit Hyperactivity Disorder (ADHD) in children aged 5 to 18 years. Cochrane Database Syst Rev. 2011(12):CD008223.

99 Abikoff H, Hechtman L, Klein RG, Gallagher R, Fleiss K, Etcovitch J, et al. Social functioning in children with ADHD treated with long-term methylphenidate and multimodal psychosocial treatment. J Am Acad Child Adolesc Psychiatry. 2004 Jul;43(7):820-9.

100 Ooi Y, Ang R. A Social Problem-Solving Skills Training Program for Aggressive Children. Korean Journal of Thinking Problem Solving. 2004;14:61-73.

101 Bloomquist ML, August GJ, Ostrander R. Effects of a school-based cognitive-behavioral intervention for ADHD children. J Abnorm Child Psychol. 1991 Oct;19(5):591-605.

102 Abikoff H, Gittelman R. Hyperactive children treated with stimulants. Is cognitive training a useful adjunct? Arch Gen Psychiatry. 1985 Oct;42(10):953-61.

103 Antshel KM, Faraone SV, Gordon M. Cognitive Behavioral Treatment Outcomes in Adolescent ADHD. J Atten Disord. 2012 May 24.

104 Antshel KM, Barkley R. Psychosocial interventions in attention deficit hyperactivity disorder. Child Adolesc Psychiatr Clin N Am. 2008 Apr;17(2):421-37, x.

105 Bateman B, Warner JO, Hutchinson E, Dean T, Rowlandson P, Gant C, et al. The effects of a double blind, placebo controlled, artificial food colourings and benzoate preservative challenge on hyperactivity in a general population sample of preschool children. Arch Dis Child. 2004 Jun;89(6):506-11.

106 McCann D, Barrett A, Cooper A, Crumpler D, Dalen L, Grimshaw K, et al. Food additives and hyperactive behaviour in 3-year-old and 8/9-year-old children in the community: a randomised, double-blinded, placebo-controlled trial. Lancet. 2007 Nov 3;370(9598):1560-7.

107 Nigg JT, Lewis K, Edinger T, Falk M. Meta-analysis of attention-deficit/hyperactivity disorder or attention-deficit/hyperactivity disorder symptoms, restriction diet, and synthetic food color additives. J Am Acad Child Adolesc Psychiatry. 2012 Jan;51(1):86-97 e8.

108 Wolraich M, Wilson D, White J. The effect of sugar on behavior or cognition in children. A meta-analysis. JAMA. 1995;274:1617-21.

109 Adesman A. Restricted elimination diet for ADHD. Lancet. 2011 May 7;377(9777):1567; author reply 8.

110 Mullins RJ, Tang ML, Dear K. Restricted elimination diet for ADHD. Lancet. 2011 May 7;377(9777):1567; author reply 8.

111 Bloch MH, Qawasmi A. Omega-3 fatty acid supplementation for the treatment of children with attention-deficit/hyperactivity disorder symptomatology: systematic review and meta-analysis. J Am Acad Child Adolesc Psychiatry. 2011 Oct;50(10):991-1000.

112 Richardson AJ, Montgomery P. The Oxford-Durham study: a randomized, controlled trial of dietary supplementation with fatty acids in children with developmental coordination disorder. Pediatrics. 2005 May;115(5):1360-6.

113 Bilici M, Yildirim F, Kandil S, Bekaroglu M, Yildirmis S, Deger O, et al. Double-blind, placebo-controlled study of zinc sulfate in the treatment of attention deficit hyperactivity disorder. Prog Neuropsychopharmacol Biol Psychiatry. 2004 Jan;28(1):181-90.

114 Akhondzadeh S, Mohammadi MR, Khademi M. Zinc sulfate as an adjunct to methylphenidate for the treatment of attention deficit hyperactivity disorder in children: a double blind and randomized trial [ISRCTN64132371]. BMC Psychiatry. 2004 Apr 8;4:9.

115 Arnold LE, Disilvestro RA, Bozzolo D, Bozzolo H, Crowl L, Fernandez S, et al. Zinc for attention-deficit/hyperactivity disorder: placebo-controlled double-blind pilot trial alone and combined with amphetamine. J Child Adolesc Psychopharmacol. 2011 Feb;21(1):1-19.

116 Ghanizadeh A, Berk M. Zinc for treating of children and adolescents with attention-deficit hyperactivity disorder: a systematic review of randomized controlled clinical trials. Eur J Clin Nutr. 2013 Jan;67(1):122-4.

117 Millichap JG, Yee MM. The diet factor in attention-deficit/hyperactivity disorder. Pediatrics. 2012 Feb;129(2):330-7.

118 Konofal E, Lecendreux M, Deron J, Marchand M, Cortese S, Zaïm M, et al. Effects of iron supplementation on attention deficit hyperactivity disorder in children. Pediatr Neurol. 2008;38.

119 Chabot RJ, Merkin H, Wood LM, Davenport TL, Serfontein G. Sensitivity and specificity of QEEG in children with attention deficit or specific developmental learning disorders. Clin Electroencephalogr. 1996 Jan;27(1):26-34.

120 Clarke AR, Barry RJ, McCarthy R, Selikowitz M. Electroencephalogram differences in two subtypes of attention-deficit/hyperactivity disorder. Psychophysiology. 2001 Mar;38(2):212-21.

121 Monastra VJ. Electroencephalographic biofeedback (neurotherapy) as a treatment for attention deficit hyperactivity disorder: rationale and empirical foundation. Child Adolesc Psychiatr Clin N Am. 2005 Jan;14(1):55-82, vi.

122 Monastra VJ, Lynn S, Linden M, Lubar JF, Gruzelier J, LaVaque TJ. Electroencephalographic biofeedback in the treatment of attention-deficit/hyperactivity disorder. Appl Psychophysiol Biofeedback. 2005 Jun;30(2):95-114.

123 Arns M, de Ridder S, Strehl U, Breteler M, Coenen A. Efficacy of neurofeedback treatment in ADHD: the effects on inattention, impulsivity and hyperactivity: a meta-analysis. Clin EEG Neurosci. 2009 Jul;40(3):180-9.

124 Loo SK, Barkley RA. Clinical utility of EEG in attention deficit hyperactivity disorder. Appl Neuropsychol. 2005;12(2):64-76.

125 Lofthouse N, Arnold LE, Hersch S, Hurt E, DeBeus R. A review of neurofeedback treatment for pediatric ADHD. J Atten Disord. 2012 Jul;16(5):351-72.

126 Willis W, Weyandt L, Lubiner A, Schubart C. Neurofeedback as a Treatment for Attention-Deficit/Hyperactivity Disorder: A Systematic Review of Evidence for Practice. Journal of Applied School Psychology. 2011;27:201-27.

127 Kasper L, Alderson R, Hudec K. Moderators of working memory deficits in children with attention-deficit/hyperactivity disorder (ADHD): a meta-analytic review. Clin Psychol Rev. 2012;32(7):605-17.

128 Martinussen R, Hayden J, Hogg-Johnsen S, Tannock R. A meta-analysis of Working memory in children with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry. 2005;44:377-84.

129 Klingberg T, Forssberg H, Westerberg H. Training of working memory in children with ADHD. J Clin Exp Neuropsychol. 2002;24:781-91.

130 Chacko A, Feirsen N, Bedard A, Marks D, Uderman J, Chimiklis A. Cogmed Working Memory Training for Youth with ADHD: A Closer Examination of Efficacy Utilizing Evidence-Based Criteria. J Clin Child Adolesc Psychol. 2013;42(6):769-83.

131 Rapport M, Orban S, Kofler M, Friedman L. Do programs designed to train working memory, other executive functions, and attention benefit children with ADHD? A meta-analytic review of cognitive, academic, and behavioral outcomes. Clin Psychol Rev. 2013;33(8):1237-52.

132 Melby-Lervag M, Hulme C. Is working memory training effective? A meta-analytic review. Dev Psychol 2013;49:270-91.

133 Chacko A, Bedard A, Marks D, Feirsen N, Uderman J, Chimiklis A, et al. A randomized clinical trial of Cogmed Working Memory Training in school-age children with ADHD: a replication in a diverse sample using a control condition. J Child Psychol Psychiatry. 2014;55(3):247-55.

134 Klingberg T. Is Working Memory capacity fixed? J Appl Res Mem Cogn. 2012;1:194-6.

135 Holmes J, Gathercole S, Dunning D. Adaptive training leads to sustained enhancement of poor working memory in children. Dev Sci. 2009;12:F2-F7.

136 Ghanizadeh A. Sensory processing problems in children with ADHD, a systematic review. Psychiatry Investig. 2011;8:89-94.

137 Ghanizadeh A, Bahrani M, Miri R, Sahraian A. Smell identification function in children with attention deficit hyperactivity disorder. Psychiatry Investig 2012;9:150-3.

138 Zimmer M, Desch L. Sensory integration therapies for children with developmental and behavioral disorders. Pediatrics 2012;129:1186-9.

139 Lan Y, Zhang L, Luo R. Attention deficit hyperactivity disorder in children: comparative efficacy of traditional Chinese medicine and methylphenidate. J Int Med Res. 2009;37:939-48.

140 Lee MS, Choi TY, Kim JI, Kim L, Ernst E. Acupuncture for treating attention deficit hyperactivity disorder: a systematic review and meta-analysis. Chin J Integr Med. 2011 Apr;17(4):257-60.

141 Li S, Yu B, Lin Z, Jiang S, He J, Kang L, et al. Randomized-controlled study of treating attention deficit hyperactivity disorder of preschool children with combined electro-acupuncture and behavior therapy. Complement Ther Med. 2010 Oct;18(5):175-83.

142 Li S, Yu B, Zhou D, He C, Kang L, Wang X, et al. Acupuncture for Attention Deficit Hyperactivity Disorder (ADHD) in children and adolescents. Cochrane Database Syst Rev. 2011(4):CD007839.

143 Khilnani S, Field T, Hernandez-Reif M, Schanberg S. Massage therapy improves mood and behavior of students with attention-deficit/hyperactivity disorder. Adolescence. 2003 Winter;38(152):623-38.

144 Field TM, Quintino O, Hernandez-Reif M, Koslovsky G. Adolescents with attention deficit hyperactivity disorder benefit from massage therapy. Adolescence. 1998 Spring;33(129):103-8.

145 Dunn FM, Howell RJ. Relaxation training and its relationship to hyperactivity in boys. J Clin Psychol. 1982 Jan;38(1):92-100.

146 Calhoun G, Jr., Bolton JA. Hypnotherapy: a possible alternative for treating pupils affected with attention deficit disorder. Percept Mot Skills. 1986 Dec;63(3):1191-5.

147 Rickson DJ, Watkins WG. Music therapy to promote prosocial behaviors in aggressive adolescent boys--a pilot study. J Music Ther. 2003 Winter;40(4):283-301.

148 Hodgkins P, Shaw M, Coghill D, Hechtman L. Amfetamine and methylphenidate medications for attention-deficit/hyperactivity disorder: complementary treatment options. Eur Child Adolesc Psychiatry. 2012 Sep;21(9):477-92.

149 Schachter HM, Pham B, King J, Langford S, Moher D. How efficacious and safe is short-acting methylphenidate for the treatment of attention-deficit disorder in children and adolescents? A meta-analysis. CMAJ. 2001 Nov 27;165(11):1475-88.

150 Abikoff H, Hechtman L, Klein RG, Weiss G, Fleiss K, Etcovitch J, et al. Symptomatic improvement in children with ADHD treated with long-term methylphenidate and multimodal psychosocial treatment. J Am Acad Child Adolesc Psychiatry. 2004 Jul;43(7):802-11.

151 Charach A, Ickowicz A, Schachar R. Stimulant treatment over five years: adherence, effectiveness, and adverse effects. J Am Acad Child Adolesc Psychiatry. 2004 May;43(5):559-67.

152 So CY, Leung PW, Hung SF. Treatment effectiveness of combined medication/behavioural treatment with chinese ADHD children in routine practice. Behav Res Ther. 2008 Sep;46(9):983-92.

153 Hechtman L, Abikoff H, Klein RG, Greenfield B, Etcovitch J, Cousins L, et al. Children with ADHD treated with long-term methylphenidate and multimodal psychosocial treatment: impact on parental practices. J Am Acad Child Adolesc Psychiatry. 2004 Jul;43(7):830-8.

154 Faraone SV. Using Meta-analysis to Compare the Efficacy of Medications for Attention-Deficit/Hyperactivity Disorder in Youths. P T. 2009 Dec;34(12):678-94.

155 Stein MA, Blondis TA, Schnitzler ER, O'Brien T, Fishkin J, Blackwell B, et al. Methylphenidate dosing: twice daily versus three times daily. Pediatrics. 1996 Oct;98(4 Pt 1):748-56.

156 Stein MA, Sarampote CS, Waldman ID, Robb AS, Conlon C, Pearl PL, et al. A dose-response study of OROS methylphenidate in children with attention-deficit/hyperactivity disorder. Pediatrics. 2003 Nov;112(5):e404.

157 Martins S, Tramontina S, Polanczyk G, Eizirik M, Swanson JM, Rohde LA. Weekend holidays during methylphenidate use in ADHD children: a randomized clinical trial. J Child Adolesc Psychopharmacol. 2004 Summer;14(2):195-206.

158 van de Loo-Neus GH, Rommelse N, Buitelaar JK. To stop or not to stop? How long should medication treatment of attention-deficit hyperactivity disorder be extended? Eur Neuropsychopharmacol. 2011 Aug;21(8):584-99.

159 Cortese S, Holtmann M, Banaschewski T, Buitelaar J, Coghill D, Danckaerts M, et al. Practitioner review: current best practice in the management of adverse events during treatment with ADHD medications in children and adolescents. J Child Psychol Psychiatry. 2013 Mar;54(3):227-46.

160 Faraone SV, Biederman J, Morley CP, Spencer TJ. Effect of stimulants on height and weight: a review of the literature. J Am Acad Child Adolesc Psychiatry. 2008 Sep;47(9):994-1009.

161 Dura-Trave T, Yoldi-Petri ME, Gallinas-Victoriano F, Zardoya-Santos P. Effects of osmotic-release methylphenidate on height and weight in children with attention-deficit hyperactivity disorder (ADHD) following up to four years of treatment. J Child Neurol. 2012 May;27(5):604-9.

162 Swanson JM, Elliott GR, Greenhill LL, Wigal T, Arnold LE, Vitiello B, et al. Effects of stimulant medication on growth rates across 3 years in the MTA follow-up. J Am Acad Child Adolesc Psychiatry. 2007 Aug;46(8):1015-27.

163 Charach A, Figueroa M, Chen S, Ickowicz A, Schachar R. Stimulant treatment over 5 years: effects on growth. J Am Acad Child Adolesc Psychiatry. 2006 Apr;45(4):415-21.

164 Moungnoi P, Maipang P. Long-term effects of short-acting methylphenidate on growth rates of children with attention deficit hyperactivity disorder at Queen Sirikit National Institute of Child Health. J Med Assoc Thai. 2011 Aug;94 Suppl 3:S158-63.

165 Kratochvil CJ, Egger H, Greenhill LL, McGough JJ. Pharmacological management of preschool ADHD. J Am Acad Child Adolesc Psychiatry. 2006 Jan;45(1):115-8.

166 Zhang H, Du M, Zhuang S. Impact of long-term treatment of methylphenidate on height and weight of school age children with ADHD. Neuropediatrics. 2010 Aug;41(2):55-9.

167 Biederman J, Spencer TJ, Monuteaux MC, Faraone SV. A naturalistic 10-year prospective study of height and weight in children with attention-deficit hyperactivity disorder grown up: sex and treatment effects. J Pediatr. 2010 Oct;157(4):635-40, 40 e1.

168 Pliszka SR, Matthews TL, Braslow KJ, Watson MA. Comparative effects of methylphenidate and mixed salts amphetamine on height and weight in children with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry. 2006 May;45(5):520-6.

169 Spencer TJ, Faraone SV, Biederman J, Lerner M, Cooper KM, Zimmerman B. Does prolonged therapy with a long-acting stimulant suppress growth in children with ADHD? J Am Acad Child Adolesc Psychiatry. 2006 May;45(5):527-37.

170 Poulton AS, Melzer E, Tait PR, Garnett SP, Cowell CT, Baur LA, et al. Growth and pubertal development of adolescent boys on stimulant medication for attention deficit hyperactivity disorder. Med J Aust. 2013 Jan 21;198(1):29-32.

171 Westover AN, Halm EA. Do prescription stimulants increase the risk of adverse cardiovascular events?: A systematic review. BMC Cardiovasc Disord. 2012;12:41.

172 Gould MS, Walsh BT, Munfakh JL, Kleinman M, Duan N, Olfson M, et al. Sudden death and use of stimulant medications in youths. Am J Psychiatry. 2009 Sep;166(9):992-1001.

173 Wilens T, McBurnett K, Stein M, Lerner M, Spencer T, Wolraich M. ADHD treatment with once-daily OROS methylphenidate: final results from a long-term open-label study. J Am Acad Child Adolesc Psychiatry. 2005 Oct;44(10):1015-23.

174 Findling RL, Wigal SB, Bukstein OG, Boellner SW, Abikoff HB, Turnbow JM, et al. Long-term tolerability of the methylphenidate transdermal system in pediatric attention-deficit/hyperactivity disorder: a multicenter, prospective, 12-month, open-label, uncontrolled, phase III extension of four clinical trials. Clin Ther. 2009 Aug;31(8):1844-55.

175 Hammerness PG, Perrin JM, Shelley-Abrahamson R, Wilens TE. Cardiovascular risk of stimulant treatment in pediatric attention-deficit/hyperactivity disorder: update and clinical recommendations. J Am Acad Child Adolesc Psychiatry. 2011 Oct;50(10):978-90.

176 Vitiello B, Elliott GR, Swanson JM, Arnold LE, Hechtman L, Abikoff H, et al. Blood pressure and heart rate over 10 years in the multimodal treatment study of children with ADHD. Am J Psychiatry. 2012 Feb;169(2):167-77.

177 Leslie LK, Cohen JT, Newburger JW, Alexander ME, Wong JB, Sherwin ED, et al. Costs and benefits of targeted screening for causes of sudden cardiac death in children and adolescents. Circulation. 2012 May 29;125(21):2621-9.

178 Bloch MH, Panza KE, Landeros-Weisenberger A, Leckman JF. Meta-analysis: treatment of attention-deficit/hyperactivity disorder in children with comorbid tic disorders. J Am Acad Child Adolesc Psychiatry. 2009 Sep;48(9):884-93.

179 Pringsheim T, Steeves T. Pharmacological treatment for Attention Deficit Hyperactivity Disorder (ADHD) in children with comorbid tic disorders. Cochrane Database Syst Rev. 2011(4):CD007990.

180 Sepulveda DR, Thomas LM, McCabe SE, Cranford JA, Boyd CJ, Teter CJ. Misuse of prescribed stimulant medication for ADHD and associated patterns of substance use: preliminary analysis among college students. J Pharm Pract. 2011 Dec;24(6):551-60.

181 Wilens TE, Adler LA, Adams J, Sgambati S, Rotrosen J, Sawtelle R, et al. Misuse and diversion of stimulants prescribed for ADHD: a systematic review of the literature. J Am Acad Child Adolesc Psychiatry. 2008 Jan;47(1):21-31.

182 Winhusen TM, Lewis DF, Riggs PD, Davies RD, Adler LA, Sonne S, et al. Subjective effects, misuse, and adverse effects of osmotic-release methylphenidate treatment in adolescent substance abusers with attention-deficit/hyperactivity disorder. J Child Adolesc Psychopharmacol. 2011 Oct;21(5):455-63.

183 Frauger E, Pauly V, Natali F, Pradel V, Reggio P, Coudert H, et al. Patterns of methylphenidate use and assessment of its abuse and diversion in two French administrative areas using a proxy of deviant behaviour determined from a reimbursement database: main trends from 2005 to 2008. CNS Drugs. 2011 May;25(5):415-24.

184 Reichow B, Volkmar F, Bloch M. Systematic review and meta-analysis of pharmacological treatment of the symptoms of attention-deficit/hyperactivity disorder in children with pervasive developmental disorders. J Autism Dev Disord. 2013;43(10):2435-41.

185 Davis N, Kollins S. Treatment for co-occurring attention deficit/hyperactivity disorder and autism spectrum disorder. Neurotherapeutics. 2012;9(3):518-30.

186 Hazell PL, Kohn MR, Dickson R, Walton RJ, Granger RE, Wyk GW. Core ADHD symptom improvement with atomoxetine versus methylphenidate: a direct comparison meta-analysis. J Atten Disord. 2011 Nov;15(8):674-83.

187 Gibson AP, Bettinger TL, Patel NC, Crismon ML. Atomoxetine versus stimulants for treatment of attention deficit/hyperactivity disorder. Ann Pharmacother. 2006 Jun;40(6):1134-42.

188 Hanwella R, Senanayake M, de Silva V. Comparative efficacy and acceptability of methylphenidate and atomoxetine in treatment of attention deficit hyperactivity disorder in children and adolescents: a meta-analysis. BMC Psychiatry. 2011;11:176.

189 van Wyk GW, Hazell PL, Kohn MR, Granger RE, Walton RJ. How oppositionality, inattention, and hyperactivity affect response to atomoxetine versus methylphenidate: a pooled meta-analysis. J Atten Disord. 2012 May;16(4):314-24.

190 Faraone SV, Biederman J, Spencer TJ, Aleardi M. Comparing the efficacy of medications for ADHD using meta-analysis. MedGenMed. 2006;8(4):4.

191 Huang YS, Tsai MH. Long-term outcomes with medications for attention-deficit hyperactivity disorder: current status of knowledge. CNS Drugs. 2011 Jul;25(7):539-54.

192 McDonagh MS, Christensen V, Peterson K, Thakurta S. Drug class review: pharmacologic treatments for attention deficit hyperactivity disorder: final report update 3 2009 Oct Disorder: Final Report Update 3.

193 McDonagh MS, Peterson K, Thakurta S, Low A. Drug cass review: pharmacologic treatments for attention deficit hyperactivity disorder: final update 4 report 2011 Dec Disorder: Final Update 4 Report.

194 Wang Y, Zheng Y, Du Y, Song DH, Shin YJ, Cho SC, et al. Atomoxetine versus methylphenidate in paediatric outpatients with attention deficit hyperactivity disorder: a randomized, double-blind comparison trial. Aust N Z J Psychiatry. 2007 Mar;41(3):222-30.

195 Donnelly C, Bangs M, Trzepacz P, Jin L, Zhang S, Witte MM, et al. Safety and tolerability of atomoxetine over 3 to 4 years in children and adolescents with ADHD. J Am Acad Child Adolesc Psychiatry. 2009 Feb;48(2):176-85.

196 Spencer TJ, Newcorn JH, Kratochvil CJ, Ruff D, Michelson D, Biederman J. Effects of atomoxetine on growth after 2-year treatment among pediatric patients with attention-deficit/hyperactivity disorder. Pediatrics. 2005 Jul;116(1):e74-80.

197 Spencer TJ, Kratochvil CJ, Sangal RB, Saylor KE, Bailey CE, Dunn DW, et al. Effects of atomoxetine on growth in children with attention-deficit/hyperactivity disorder following up to five years of treatment. J Child Adolesc Psychopharmacol. 2007 Oct;17(5):689-700.

198 Michelson D, Faries D, Wernicke J, Kelsey D, Kendrick K, Sallee FR, et al. Atomoxetine in the treatment of children and adolescents with attention-deficit/hyperactivity disorder: a randomized, placebo-controlled, dose-response study. Pediatrics. 2001 Nov;108(5):E83.

199 Wernicke JF, Faries D, Girod D, Brown J, Gao H, Kelsey D, et al. Cardiovascular effects of atomoxetine in children, adolescents, and adults. Drug Saf. 2003;26(10):729-40.

200 Spencer T, Biederman J, Heiligenstein J, Wilens T, Faries D, Prince J, et al. An open-label, dose-ranging study of atomoxetine in children with attention deficit hyperactivity disorder. J Child Adolesc Psychopharmacol. 2001 Fall;11(3):251-65.

201 Kratochvil CJ, Wilens TE, Greenhill LL, Gao H, Baker KD, Feldman PD, et al. Effects of long-term atomoxetine treatment for young children with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry. 2006 Aug;45(8):919-27.

202 Dittmann RW, Schacht A, Helsberg K, Schneider-Fresenius C, Lehmann M, Lehmkuhl G, et al. Atomoxetine versus placebo in children and adolescents with attention-deficit/hyperactivity disorder and comorbid oppositional defiant disorder: a double-blind, randomized, multicenter trial in Germany. J Child Adolesc Psychopharmacol. 2011 Apr;21(2):97-110.

203 Thurstone C, Riggs PD, Salomonsen-Sautel S, Mikulich-Gilbertson SK. Randomized, controlled trial of atomoxetine for attention-deficit/hyperactivity disorder in adolescents with substance use disorder. J Am Acad Child Adolesc Psychiatry. 2010 Jun;49(6):573-82.

204 Patel BD, Barzman DH. Pharmacology and Pharmacogenetics of Pediatric ADHD with Associated Aggression: A Review. Psychiatr Q. 2013 Feb 27.

205 Pringsheim T, Gorman D. Second-generation antipsychotics for the treatment of disruptive behaviour disorders in children: a systematic review. Can J Psychiatry. 2012 Dec;57(12):722-7.

206 Van Bellinghen M, De Troch C. Risperidone in the treatment of behavioral disturbances in children and adolescents with borderline intellectual functioning: a double-blind, placebo-controlled pilot trial. J Child Adolesc Psychopharmacol. 2001 Spring;11(1):5-13.

207 Aman MG, De Smedt G, Derivan A, Lyons B, Findling RL. Double-blind, placebo-controlled study of risperidone for the treatment of disruptive behaviors in children with subaverage intelligence. Am J Psychiatry. 2002 Aug;159(8):1337-46.

208 Armenteros JL, Lewis JE, Davalos M. Risperidone augmentation for treatment-resistant aggression in attention-deficit/hyperactivity disorder: a placebo-controlled pilot study. J Am Acad Child Adolesc Psychiatry. 2007 May;46(5):558-65.

209 List BA, Barzman DH. Evidence-based recommendations for the treatment of aggression in pediatric patients with attention deficit hyperactivity disorder. Psychiatr Q. 2011 Mar;82(1):33-42.

210 Palumbo DR, Sallee FR, Pelham WE, Jr., Bukstein OG, Daviss WB, McDermott MP. Clonidine for attention-deficit/hyperactivity disorder: I. Efficacy and tolerability outcomes. J Am Acad Child Adolesc Psychiatry. 2008 Feb;47(2):180-8.

211 Sallee FR, Kollins SH, Wigal TL. Efficacy of guanfacine extended release in the treatment of combined and inattentive only subtypes of attention-deficit/hyperactivity disorder. J Child Adolesc Psychopharmacol. 2012 Jun;22(3):206-14.

212 Jain R, Segal S, Kollins SH, Khayrallah M. Clonidine extended-release tablets for pediatric patients with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry. 2011 Feb;50(2):171-9.

213 Daviss WB, Patel NC, Robb AS, McDermott MP, Bukstein OG, Pelham WE, Jr., et al. Clonidine for attention-deficit/hyperactivity disorder: II. ECG changes and adverse events analysis. J Am Acad Child Adolesc Psychiatry. 2008 Feb;47(2):189-98.

214 Scahill L. Alpha-2 adrenergic agonists in children with inattention, hyperactivity and impulsiveness. CNS Drugs. 2009;23 Suppl 1:43-9.

215 Jafarinia M, Mohammadi MR, Modabbernia A, Ashrafi M, Khajavi D, Tabrizi M, et al. Bupropion versus methylphenidate in the treatment of children with attention-deficit/hyperactivity disorder: randomized double-blind study. Hum Psychopharmacol. 2012 Jul;27(4):411-8.

216 Spencer T, Biederman J, Steingard R, Wilens T. Bupropion exacerbates tics in children with attention-deficit hyperactivity disorder and Tourette's syndrome. J Am Acad Child Adolesc Psychiatry. 1993 Jan;32(1):211-4.

217 Rapport MD, Carlson GA, Kelly KL, Pataki C. Methylphenidate and desipramine in hospitalized children: I. Separate and combined effects on cognitive function. J Am Acad Child Adolesc Psychiatry. 1993 Mar;32(2):333-42.

218 Garfinkel BD, Wender PH, Sloman L, O'Neill I. Tricyclic antidepressant and methylphenidate treatment of attention deficit disorder in children. J Am Acad Child Psychiatry. 1983 Jul;22(4):343-8.

219 Pliszka SR. Tricyclic antidepressants in the treatment of children with attention deficit disorder. J Am Acad Child Adolesc Psychiatry. 1987 Mar;26(2):127-32.

220 Quintero J, Lopez-Munoz F, Alamo C, Loro M, Garcia-Campos N. Reboxetine for ADHD in children non-responders or with poor tolerance to methylphenidate: a prospective long-term open-label study. Atten Defic Hyperact Disord. 2010 Nov;2(3):107-13.

221 Mahmoudi-Gharaei J, Dodangi N, Tehrani-Doost M, Faghihi T. Duloxetine in the treatment of adolescents with attention deficit/hyperactivity disorder: an open-label study. Hum Psychopharmacol. 2011 Mar;26(2):155-60.

222 Carlson GA, Dunn D, Kelsey D, Ruff D, Ball S, Ahrbecker L, et al. A pilot study for augmenting atomoxetine with methylphenidate: safety of concomitant therapy in children with attention-deficit/hyperactivity disorder. Child Adolesc Psychiatry Ment Health. 2007;1(1):10.

223 Treuer T, Gau SS, Mendez L, Montgomery W, Monk JA, Altin M, et al. A systematic review of combination therapy with stimulants and atomoxetine for attention-deficit/hyperactivity disorder, including patient characteristics, treatment strategies, effectiveness, and tolerability. J Child Adolesc Psychopharmacol. 2013 Apr;23(3):179-93.

224 Kollins SH, Jain R, Brams M, Segal S, Findling RL, Wigal SB, et al. Clonidine extended-release tablets as add-on therapy to psychostimulants in children and adolescents with ADHD. Pediatrics. 2011 Jun;127(6):e1406-13.

225 Wilens TE, Bukstein O, Brams M, Cutler AJ, Childress A, Rugino T, et al. A controlled trial of extended-release guanfacine and psychostimulants for attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry. 2012 Jan;51(1):74-85 e2.

226 Adler LD, Nierenberg AA. Review of medication adherence in children and adults with ADHD. Postgrad Med. 2010 Jan;122(1):184-91.

227 Pescosolido BA, Jensen PS, Martin JK, Perry BL, Olafsdottir S, Fettes D. Public knowledge and assessment of child mental health problems: findings from the National Stigma Study-Children. J Am Acad Child Adolesc Psychiatry. 2008 Mar;47(3):339-49.

228 Hansen DL, Hansen EH. Caught in a balancing act: parents' dilemmas regarding their ADHD child's treatment with stimulant medication. Qual Health Res. 2006 Nov;16(9):1267-85.

229 Brinkman WB, Sherman SN, Zmitrovich AR, Visscher MO, Crosby LE, Phelan KJ, et al. Parental angst making and revisiting decisions about treatment of attention-deficit/hyperactivity disorder. Pediatrics. 2009 Aug;124(2):580-9.

230 Coletti DJ, Pappadopulos E, Katsiotas NJ, Berest A, Jensen PS, Kafantaris V. Parent perspectives on the decision to initiate medication treatment of attention-deficit/hyperactivity disorder. J Child Adolesc Psychopharmacol. 2012 Jun;22(3):226-37.

231 Wong IC, Asherson P, Bilbow A, Clifford S, Coghill D, DeSoysa R, et al. Cessation of attention deficit hyperactivity disorder drugs in the young (CADDY)--a pharmacoepidemiological and qualitative study. Health Technol Assess. 2009 Oct;13(50):iii-iv, ix-xi, 1-120.

232 Greenhill L, Kollins S, Abikoff H, McCracken J, Riddle M, Swanson J, et al. Efficacy and safety of immediate-release methylphenidate treatment for preschoolers with ADHD. J Am Acad Child Adolesc Psychiatry. 2006 Nov;45(11):1284-93.

233 Abikoff HB, Vitiello B, Riddle MA, Cunningham C, Greenhill LL, Swanson JM, et al. Methylphenidate effects on functional outcomes in the Preschoolers with Attention-Deficit/Hyperactivity Disorder Treatment Study (PATS). J Child Adolesc Psychopharmacol. 2007 Oct;17(5):581-92.

234 Ghuman JK, Arnold LE, Anthony BJ. Psychopharmacological and other treatments in preschool children with attention-deficit/hyperactivity disorder: current evidence and practice. J Child Adolesc Psychopharmacol. 2008 Oct;18(5):413-47.

235 Swanson J, Greenhill L, Wigal T, Kollins S, Stehli A, Davies M, et al. Stimulant-related reductions of growth rates in the PATS. J Am Acad Child Adolesc Psychiatry. 2006 Nov;45(11):1304-13.

236 Wigal T, Greenhill L, Chuang S, McGough J, Vitiello B, Skrobala A, et al. Safety and tolerability of methylphenidate in preschool children with ADHD. J Am Acad Child Adolesc Psychiatry. 2006 Nov;45(11):1294-303.

237 Wu EQ, Hodgkins P, Ben-Hamadi R, Setyawan J, Xie J, Sikirica V, et al. Cost effectiveness of pharmacotherapies for attention-deficit hyperactivity disorder: a systematic literature review. CNS Drugs. 2012 Jul 1;26(7):581-600.

238 King S, Griffin S, Hodges Z, Weatherly H, Asseburg C, Richardson G, et al. A systematic review and economic model of the effectiveness and cost-effectiveness of methylphenidate, dexamfetamine and atomoxetine for the treatment of attention deficit hyperactivity disorder in children and adolescents. Health Technol Assess. 2006 Jul;10(23):iii-iv, xiii-146.

239 Jensen PS, Garcia JA, Glied S, Crowe M, Foster M, Schlander M, et al. Cost-effectiveness of ADHD treatments: findings from the multimodal treatment study of children with ADHD. Am J Psychiatry. 2005 Sep;162(9):1628-36.

240 Pliszka S, Bernet W, Bukstin O, Walter H. Practice parameter for the assessment and treatment of children and adolescents with attention-deficit/ hyperactivity disorder. J Am Acad Child Adolesc Psychiatry. 2007;46:894 - 921.

241 Taylor D, Paton C, Kapur S. The Maudsley Prescribing Guidelines in Psychiatry, 11th Edition: Wiley-Blackwell; 2012.

242 Greydanus D, Nazeer A, Patel D. Psychopharmacology of ADHD in pediatrics: Current advances and issues. Neuropsychiatric Disease and Treatment. 2009;5:171 - 81.

243 Institute of Clinical System Improvement. Health Care Guideline - Diagnosis and Management of Attention Deficit Hyperactivity Disorder in Primary Care for School-Age Children and Adolescents. 9th Edition: Institute of Clinical System Improvement; 2012.

244 Hosenbocus S, Chahal R. A review of long-acting medications for ADHD in Canada. J Can Acad Child Adolesc Psychiatry. 2009;18:331 - 9.

245 Findling R, Childress A, Cutler A, Gasior M, Hamdani M, Ferreira-Cornwell C, et al. Efficacy and safety of lisdexamfetamine dimesylate in adolescents with attention-deficit/ hyperactivity disorder. J Am Acad Child Adolesc Psychiatry. 2011;50:395 - 405

246 Vaughan B, Fegerr J, Kratochvil C. Update on atomoxetine in the treatment of attention-deficit/ hyperactivity disorder. Expert Opin Pharmacother. 2009;10:669 - 76.

247 Findling R, Turnbow J, Burnside J, Melmed R, Civil R, Li Y. A randomized, double-blind, multicenter, parallel group, placebo-controlled, dose optimization study of the methylphenidate transdermal system for the treatment of ADHD in adolescents. CNS Spectr. 2010;15:419 - 30.

248 Michelson D, Adler L, Spencer T, Reimherr F, West S, Allen A, et al. Atomoxetine in adults with ADHD: Two randomized, placebo-controlled studies. Biological psychiatry. 2003;53:112 - 20.

249 Wilens T, Bukstein O, Brams M, Cuttler A, Childress A, Rugino T, et al. A controlled trial of extended-relaseguanfacine and psychostimulants for attention-deficit/ hyperactivity disorder. J Am Acad Child Adolesc Psychiatry. 2012; 51:74 - 85.

250 Andrew P, Nakamura H, Reed M. Child and adolescent psychopharmacology: Drug-drug interactions in pediatric psychopharmacology. Pediatric Clinic of North America. 1998;45:1233 - 64.

## Self-assessment (MCQs)

After reading the Clinical Practice Guidelines, you can claim one CME point under Category 3A (Self-Study) of the SMC Online CME System. Alternatively, you can claim one CME point under Category 3B (Distance Learning - Verifiable Self-Assessment) if you answer at least 60% of the following MCQs correctly. You can submit your answers through the SMJ website at this link: http://sma.org.sg/publications/index.aspx?ID=26 *(the link will only be available once the August 2014 issue of the SMJ becomes available)*. The answers will be published in the SMJ October 2014 issue and at the MOH webpage for these guidelines after the period for submitting the answers is over.

*Instruction: Choose True or False for each statement.*

| | | True | False |
|---|---|---|---|
| 1. | ADHD can be diagnosed when: | | |
| | A) The child meets the symptom checklist as required by DSM or ICD. | ☐ | ☐ |
| | B) Both parents and teachers rate the child with high scores on a standard rating scale. | ☐ | ☐ |
| | C) A thorough clinical history from parents and teachers or other caregivers fulfills all DSM or ICD criteria. | ☐ | ☐ |
| | D) A child has been observed to exhibit symptoms in a clinic setting. | ☐ | ☐ |
| 2. | Recognised risks associated with methylphenidate use include: | | |
| | A) Reduced appetite. | ☐ | ☐ |
| | B) Reduced rate of physical growth. | ☐ | ☐ |
| | C) Increased cardiovascular risk. | ☐ | ☐ |
| | D) Risk of medication abuse or diversion. | ☐ | ☐ |

| | | True | False |
|---|---|---|---|
| 3. | Features present in all cases of ADHD include: | | |
| | A) Symptoms present before the age of 7. | ☐ | ☐ |
| | B) Significant hyperactive and/or impulsive symptoms. | ☐ | ☐ |
| | C) Significant impairment from the symptoms. | ☐ | ☐ |
| | D) Presence of symptoms in more than one setting. | ☐ | ☐ |
| 4. | Regarding treatment for ADHD: | | |
| | A) Methylphenidate should be used when ADHD is of at least moderate severity. | ☐ | ☐ |
| | B) Parent training should be offered when a pre-schooler is diagnosed with ADHD. | ☐ | ☐ |
| | C) Behaviour treatment is useful when there is significant comorbid anxiety symptom. | ☐ | ☐ |
| | D) Methylphenidate should be considered when there is comorbid oppositional defiant disorder or conduct disorder. | ☐ | ☐ |
| 5. | If a parent is not keen to have the child receive medication for the treatment of ADHD, the following will be reasonable next strategies: | | |
| | A) Educate about behavioural management strategies. | ☐ | ☐ |
| | B) Refer for neurofeedback therapy. | ☐ | ☐ |
| | C) Suggest parent communicate the diagnosis to the school teachers and seek their help. | ☐ | ☐ |
| | D) Educate teachers about classroom management strategies, at least in writing. | ☐ | ☐ |

## Workgroup members

The members of the workgroup, who were appointed in their personal professional capacity, are:

**Chairman**

A/Prof Daniel Fung
Chairman, Medical Board and Senior Consultant
Institute of Mental Health

**Members (in alphabetical order)**

Dr Lim Choon Guan
Consultant and Deputy Chief
Department of Child & Adolescent Psychiatry
Institute of Mental Health

A/Prof John Wong Chee Meng
Head and Senior Consultant
Department of Psychological Medicine
Yong Loo Ling School of Medicine
NUS and National University Hospital

Dr Ng Koon Hock
Psychiatrist
The Psychotherapy Clinic for Adults and Children

Dr Cheok Cheng Soon Christopher
Deputy Chairman Medical Board
Head of Department & Senior Consultant
Psychological Medicine
Khoo Teck Puat Hospital

Dr Jennifer Kiing Sie Hee
Consultant
Child Development Unit
Department of Paediatrics
Khoo Teck Puat – National University Children's Medical Institute and National University Hospital

Dr Chong Shang Chee
Head & Consultant
Child Development Unit
Department of Paediatrics
Khoo Teck Puat – National University Children's Medical Institute and National University Hospital

Dr June Lou
Consultant Paediatrician
Ovspring Developmental Clinic

**Members**

A/Prof Mary Lourdes Daniel
Senior Consultant & Head of
Clinical Services
Department of Child Development
Senior Consultant & Director
Universal Newborn Hearing Program
Department of Neonatology
KK Women's & Children's Hospital

Dr Desmond Ong
Family Physician
Jurong Polyclinic
NHG Polyclinics

Dr Charity Low
Family Physician
Peace Family Clinic (WL 832) Pte
Ltd

Dr Sharifah Mariam Aljunied
Principal Specialist (Educational
Psychology)
Education Services Division
Ministry Of Education

Mr Choi Pui Meng
Senior Specialist
Educational Psychology
Ministry of Education

Ms Kala Mehrotra
Principal Educational Psychologist
Department of Child and Adolescent
Psychiatry
Institute of Mental Health

Ms Carolyn Kee
Principal Psychologist
Department of Child and Adolescent
Psychiatry
Institute of Mental Health

Ms Ivy Leung
Senior Occupational Therapist
Institute of Mental Health

Ms Yen Lee Chen
Senior Pharmacist
Institute of Mental Health

Ms Geraldine Wong
Principal Medical Social Worker
Department of Child and Adolescent
Psychiatry
Institute of Mental Health

APN Lee Poh Yin
Advanced Practice Nurse
REACH (West)
Department of Psychological
Medicine, National University
Hospital

Mrs Bella Chin
President
Society for the Promotion of ADHD
Research and Knowledge (SPARK)

Ms Ng Hwee Chien
Senior Guidance Specialist
Guidance Branch, Student
Development Curriculum Division
Ministry of Education

**Acknowledgments**

The workgroup would like to acknowledge the time and effort of the following independent expert referees who are experienced clinicians or researchers. They were asked to review and comment on the draft version of the clinical practice guidelines and all of them provided important comments which were addressed by the workgroup. The workgroup is grateful for their time and effort in helping to complete this guideline. These expert referees are:

Dr Gordon Harper
Associate Professor of Psychiatry
Harvard Medical School

Dr Scott H. Kollins
Professor & Vice-Chair for Research Strategy & Development
Director, Duke ADHD Program
Department of Psychiatry & Behavioral Sciences
Professor, Department of Psychology & Neuroscience
Duke University, Durham, NC

Dr Rosemary Tannock
Professor Emeritus
Ontario Institute of Studies in Education, University of Toronto
Senior Scientist
Neurosciences & Mental Health Research Program
Research Institute of the Hospital for Sick Children

Dr Toh Chin Lee
Senior Consultant Child and Adolescent Psychiatrist &
Head of Department of Psychiatry
Hospital Selayang

The workgroup would also like to acknowledge the following:

**Subsidiary editors:**

Dr Pwee Keng Ho
Deputy Director (Health Technology Assessment)
Performance & Technology Assessment Division
Ministry of Health

Mr Raymond Huang
Manager (Health Technology Assessment)
Performance & Technology Assessment Division
Ministry of Health

**Secretariat team:**

Ms Chin Mien Chew
Information Specialist (Health Technology Assessment)
Performance & Technology Assessment Division
Ministry of Health

Ms Suriana Taib
Manager (Health Technology Assessment)
Performance & Technology Assessment Division
Ministry of Health


Dr Edwin Chan Shih-Yen
Head, Epidemiology
Singapore Clinical Research Institute
Assoc Professor, Duke-NUS Graduate Medical School, Singapore
Director, Singapore Branch, Australasian Cochrane Centre;
Head (Evidence-based Medicine)
Performance & Technology Assessment Division
Ministry of Health

**These organisations have commented on and endorsed the guidelines (in alphabetical order):**

Academy of Medicine, Singapore
Chapter of Psychiatrists, Academy of Medicine, Singapore
College of Paediatrics and Child Health, Singapore
College of Family Physicians Singapore